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THE NUTRITION OF PATIENTS WITH THERMAL BURNS

STANLEY M. LEVENSON, M.D., CHARLES S. DAVIDSON, M.D., C.M.,
CHARLES C. LUND, M.D., F.A.C.S., and F. H. L. TAYLOR, Ph.D., Boston, Massachusetts

LOSS of weight, often marked, has long been recognized as a serious complication in severely burned patients. However, only in recent years has the problem of maintaining the nutrition of these patients been clearly recognized. With the increased use of plasma and the reemphasis of the proper use of electrolyte solutions, many of the severely burned patients who formerly died of circulatory collapse are being brought through the early shock phase into the later period frequently characterized by marked nutritional disturbances. Thus, the problem of malnutrition following thermal injury which was hitherto seen only occasionally must now be faced in an increasing number of patients.

The excess loss of nitrogenous products in the urine (9, 28, 42) and from the burned surfaces (24) together with the progressive reduction in plasma protein concentration (39, 42) indicate that actual body protein is depleted in these patients. Attempts to combat the weight loss by high caloric, high vitamin, and high protein diets have frequently been made in such patients (1), but there are few detailed studies of the actual nutritional requirements (14, 24, 43). The most recent report is that of CoTui (15) on 3 patients with third degree burns of varying severity. The present communication is concerned with a group of 32 individuals studied in the period November, 1942, to August, 1943, in each of whom an effort was made to determine, and in some cases to meet, the protein and caloric requirements, and to ascertain to what extent factors such as age, nutritional status on entry, and extent of third degree burn influenced the food requirement. In addition, the problem of late liver damage is discussed.

From the Thorndike Memorial Laboratory, the Second and Fourth Medical Services (Harvard) and the Burn Assignment of the Surgical Services, Boston City Hospital, and the Departments of Medicine and Surgery, Harvard Medical School.

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METHODS

The food intake in terms of calories, protein, carbohydrate, and fat was determined from records of the food ingested by the patients using standard tables (7). In several patients whose protein and caloric intake changed very little during certain periods of their course, these figures were averaged. This was done in preparing the data for Chart 1 (after the second week), Chart 3 (after the twelfth week) and Chart 4 (after the eighth week). It was considered more representative of the facts to present the data in this way since the week to week variations were less than the errors inherent in the calculations.

The daily urinary nitrogen excretion was determined by the micro-Kjeldahl method. Total plasma protein, albumin-globulin fractionations and nonprotein nitrogen determinations were made by the Howe method (26). Plasma protein concentration below 5.0 grams per 100 milliliters was considered hypoproteinemia; albumin below 2.5 and globulin above 3.0 were considered abnormal. Hemoglobin was determined by the Klett-Summerson colorimeter using 15.6 grams of hemoglobin per 100 cubic centimeters of blood as 100 per cent. The icteric index of the plasma was determined by comparison with dichromate standards (29). Prothrombin concentration was determined by a modification (36) of the method of Quick. Cephalin flocculation (22) and hippuric acid excretion after ingestion of sodium benzoate (34) were studied in a few patients.[1]

Approximate admission weights were obtained by history. The patients were not weighed during the early acute period but weights were determined in the later stages of recovery or at autopsy.

METHODS OF SUPPLYING FOOD

During the first few days following injury most of the severely burned patients refused solid food and were given liquids by mouth. As soon as possible they were urged to take a solid diet. The diets used are shown in Table I. The burn diet was made by supplementing the house diet with foods rich in protein and fat. A few patients in whom a special study of anemia was made were given a diet free of liver but otherwise similar to the burn diet. All patients receiving the burn diet were given varying amounts of eggnog supplement, the formula for which is given in Table I. Some patients in whom it was judged that the oral intake was insufficient were given supplements by stomach tube or intravenously. The mixture used for tube feeding was similar to the regular eggnog supplement but with the addition of ground fresh liver. The mixture was given in amounts of 100 to 150 cubic centimeters an hour. The intravenous supplement was an acid casein hydrolysate. It was given as a 5 per cent solution in 5 per cent glucose in amounts up to 150 grams of hydrolysate daily. The mixture may be given intrasternally (47). The sternal needle designed by Turkel (44) has been found satisfactory.

No study of the vitamin requirements of these patients was made. Vitamin supplements were given to all patients. In the early cases the amounts of this supplementation were irregular, but later a standard dosage was made of about 5 times the recommended daily allowances of the Committee on Food and Nutrition of the National Research Council (13) in the form of concentrates (vitamins A and D), pure vitamins (thiamin, nicotinic acid amide, riboflavin, and ascorbic acid) and brewer's yeast. In addition, 50 milligrams of calcium pantothenate and 50 milligrams of pyridoxine were given.

The estimation of the areas involved by burn was made according to Berkow's tables (6). These estimates were made on admission in the case of total area burned, but not until sloughing was complete for the areas involved in third degree burns.

RESULTS

General clinical features. Tables II and III present the pertinent data of the 32 patients. They are divided into two classes according to the extent of deep burn: Class I being made up of those patients with less than 10 per cent third degree burn, and Class II of those with 10 per cent or more third degree burn.

Each of these classes is further divided into two groups according to the state of the patient's nutrition on admission. The first group is made up of those whose nutrition was considered good, because they gave histories of good food intakes, were well nourished, and showed no evidence of nutritional deficiencies. The second group contains those who gave histories of inadequate food intake and showed evidences of malnutrition. Many of the latter patients were chronic alcoholics. Twenty-one of the patients were burned at the Cocoanut Grove Night Club fire while 11 were burned on separate occasions subsequent to this disaster. Twelve had clinical evidence of shock and all but 4 were given blood plasma during the first 24 hours in amounts varying from 250 milliliters to 5 liters.

[1]Courtesy of Dr. Stephen J. Maddock, Boston City Hospital.

Many of the patients burned at the Cocoanut Grove fire and a few of those burned subsequently suffered varying degrees of respiratory tract injury (19). The data do not show that this complication, which was relatively short lived, significantly influenced subsequent nutritional requirements. Most of the patients received systemic sulfadiazine therapy for varying periods of time.

The patients are divided in regard to fever from 0 (afebrile) to 4: (1) those with temperatures up to 101 degrees F. for less than a week; (2) those with temperatures up to 102 degrees F. for more than 2 days but less than a week; (3) those with temperatures up to 103 degrees for 1 to 2 weeks; and (4) those with temperatures of greater than 101 degrees F. for over a month.

Inspection of Table II reveals that, in the less severe burns, fever, although present in every instance, was not a serious occurrence and was roughly related to the extent of burn. There were 3 instances of sensitivity to sulfadiazine as evidenced by fever. In only one instance (Case 7) was this type of fever significant in height or duration. The patients in Class II (severe burns) (Table III) had more fever than those in Class I.

Wound infection developed in every instance of third degree burn. Cultures revealed a mixture of organisms with hemolytic Staphylococcus aureus being most common. No accurate measure was made of the amount of exudation from the burn surface, but an estimation was made in each instance and the amount recorded as 1 to 4 plus. In general, the greater the area of full thickness burn, the greater was the amount of exudate. In addition, it was noted that there was considerably more exudation from the unhealthy, edematous granulations of the poorly nourished patients than from the firm, healthy appearing granulations of the well nourished individuals.

The occurrence of progressive anemia necessitating frequent blood transfusions was closely related to the severity of the burn. Among the patients in Class I there were 6 instances of anemia (Cases 9, 10, 13, 14, 15, and 18). All of these patients were female. It should be noted that all the females but no males in this class developed anemia. In contrast, all but 2 patients (Cases 21 and 28) in Class II became anemic.

TABLE I.—DIETS AND FORMULA*

Diets	Protein gm.	N. gm.	Carbo. gm.	Fat gm.	Total calories
House diet	90	13	250	50	1800
Burn diet	140	21	220	100	2350
Eggnog supplement (1.5 liters)	135	22	367	7	2050
Intubation formula (1.5 liters)	153	24	373	17	2250
For mulas** Eggnog (1.5 liters)					
8 eggs whites	35	5.6	0	1	
32 ounces skim milk	32	5.1	48	4	
4 ounces orange juice	0	0	12	0	
3 tablespoons brewer's yeast	24	3.8	19	1	
20 tablespoons casec	44	7.0	0	1	
10 ounces lactose	0	0	288	0	
Total	135	21.5	367	7	2050
Intubation (1.5 liters)					
6 egg whites	26	4.0	0	1	
32 ounces skim milk	32	5.1	48	4	
4 ounces orange juice	0	0	12	0	
3 tablespoons brewer's yeast	24	3.8	19	1	
20 tablespoons casec	44	7.0	0	1	
10 ounces lactose	0	0	288	0	
4 ounces raw liver (ground)	27	4.0	6	10	
Total	153	23.9	373	17	2250

*Our thanks are due to Miss Lynch, chief dietitian and to Miss Levy, Miss Rubinoff and Miss Trainovich for their untiring efforts in suggesting, preparing, and calculating diets.

**The eggnog and intubation formulas are modifications of a formula suggested by Dr. Frederick J. Stare, Harvard Medical School.

Metabolic and nutritional considerations. Class I. Moderate burns. The 15 patients in *good nutritional status* on admission presented only mild nutritional problems. Food intake was low during the first week in all but one (Case 8). Thereafter all but 2 were able to take food containing from 100 to 180 grams of protein daily and 2,000 to 3,500 calories. The 2 exceptions (Cases 2 and 5) ate poorly during the second week because of mental depression and a severe pharyngitis, respectively, but from then on both had food intakes similar to the other patients in this group. The urinary nitrogen excretion was somewhat elevated in a few instances but was not excessive or prolonged except in one patient (Case 7). Progressive hypoproteinemia was not seen. However, 6 patients had temporary

TABLE II.—CLASS I. PATIENTS WITH MODERATE BURNS

No. Age Sex	Per cent body surface burned Total 3d degree	Chronic alcoholism	Complications				Diet				Nitrogen excretion		Plasma protein concentration gm./100 ml.	Discharge day	Result
			Fever§	Local exudation¶	Anemia	Liver disease	Time (weeks)	Average calories	Daily food intake: Protein (grams)	Daily food intake: Nitrogen (grams)	Time (weeks)	Average daily urinary nitrogen (grams)			
1* 22 M	6 0	0	1	1	0	0	1	1400	70	11	1	17	Total+A. G. Normal throughout	23**	Lived
							2	3200	140	22	2	14			
							3+	3700	180	29	3	17			
2* 20 M	6 0	0	2	1	0	0	1	1400	70	11	1	11	Total+A. G. Normal throughout	17**	Lived
							2	1600	80	13	2	10			
							3+	2700	120	19	3				
3* 44 M	6 1	0	2	1	0	0	1	1400	70	11	1	11	Total+A. G. Normal throughout	30**	Lived
							2	2500	120	19	2	11			
							3+	3000	130	21	3	7			
4* 25 M	6 1	0	1	1	0	0	1	1400	70	11	1	16	Total+A. G. Normal throughout	17**	Lived
							2	2500	125	20	2	13			
							3+	3000	135	22	3				
5* 23 M	6 1	0	2▲	1	0	0	1	1200	60	9.6	1	14	Total+A. G. Normal throughout	60**	Lived
							2	1200	60	9.6	2	10			
							3+	2700	120	19	3+	9			
6* 50 M	6 1	0	1	1	0	0	1	1400	70	11	1	16	Total+A. G. Normal throughout	20**	Lived
							2	3200	130	21	2	11			
							3+	3500	140	22	3+	12			
7* 35 M	6 2	0	3▲	1	0	0	1	1400	70	11	1	14	Total normal throughout A.2.4, G.4.3. (Drug fever during 2d week; normal thereafter	31**	Lived
							2	2500	100	8.6	2	20			
							3+	3000	150	24	3+	14			
8* 11 M	8 2	0	0	1	0	0	1	3200	130	21	1	11	Total+A. G. Normal throughout	64**	Lived
							2	3500	140	22	2	11			
							3+	3500	140	22	3	8			
											4	9			
9* 67 F	15 3	0	3	2	+	0	1	2000	90	14	1	9	See Chart 1	80**	Lived
							2	2000	120	19	2	7			
							3+	2700	125	20	3	7			
											4	7			
10* 30 F	8 3	0	1	1	+	0	1	1400	70	11	1	11	Total+A. G. Normal throughout	113**	Lived
							2	2500	120	19	2	10			
							3+	2500	125	20	3	7			
											4	7			
11* 33 M	8 4	0	2	1	0	0	1	1400	70	11	1	13	Total normal throughout A.2.4, G.3.0 during 1st 2 weeks. Normal thereafter	28**	Lived
							2	3200	148	24	2	16			
							3+	2600	140	22	3	19			
											4	13			

*Nutritional status on admission—good.
†Nutritional status on admission—fair.
‡Nutritional status on admission—poor.
**Nutritional status on discharge—good.
††Nutritional status on discharge—fair.
‡‡Nutritional status on discharge—poor.

§Fever: 0, Afebrile; 1, temperature up to 101 degrees for less than 1 week; 2, temperature up to 102 degrees for more than 2 days but less than 1 week; 3, temperature up to 103 degrees for 1 to 2 weeks; 4, temperature greater than 101 degrees for over 1 month.
▲Fever from sulfonamide treatment.
¶Local exudation: (1) slight, (2) moderate, (3) severe, (4) very severe.

TABLE II.—CLASS I. PATIENTS WITH MODERATE BURNS—Continued

No. Age Sex	Per cent body surface burned Total	3d degree	Chronic alcoholism	Complications: Fever§	Local exudation¶	Anemia	Liver disease	Diet: Time (weeks)	Average calories	Daily food intake: Protein (grams)	Nitrogen (grams)	Nitrogen excretion: Time (weeks)	Average daily urinary nitrogen (grams)	Plasma protein concentration gm./100 ml.	Discharge day	Result
12* 30 M	16	2	0	2	1	0	0	1	1400	70	11	1	11	Total normal throughout. 2d week A. 2.7, G. 3.1. Normal thereafter	35**	Lived
								2	2500	125	20	2	10			
								3+	3200	140	22	3	7			
13* 27 F	25	5	0	2	2	+	0	1	1400	70	11	1	8	Total normal throughout. 4th week, A.2.6, G. 2.9. Normal throughout	87**	Lived
								2	2500	120	19	2	9			
								3+	3000	130	21	3	10			
												4	8			
14* 28 F	13	7	0	3	1	+	0	1	1400	70	11	1		Total+A. G. Normal throughout	155**	Lived
								2	2200	110	18	2				
								3+	3000	125	20	3				
15* 30 F	20	7	0	2	2	+	0	1	1400	70	11	1	11	Total normal throughout. A fell to 2.4, G. rose to 3.0 in 2d week and to 4.1 by the 6th week. By 22d week A. up to 3.6, G down to 3.3	197††	Lived
								2	2000	100	16	2	10			
								3+	3000	120	19	3	7			
16† 59 M	6	5	+	2^	2	0	0	1	2000	90	14	1	16	Total+A. G. Normal throughout	81**	Lived
								2	4000	160	26	2	11			
								3+	4500	160	26	3	11			
												4	11–15			
17‡ 31 M	8	5	+	3	2	0	0	1	1200	60	9.6	1	—	Total+A. G. Normal throughout	66**	Lived
								2	1200	60	9.6	2	—			
								3+	3500	150	24	3	—			
18‡ 75 F	10	8	0	2	2	+	0	1	1700	90	14.4	1		Total+A. G. Normal until 4th week; total then fell to 4.4. A.2.5, G. 1.0	32‡‡	Died
								2	1700	90	14.4	2				
								3+	1700	90	14.4	3				

*Nutritional status on admission—good.
†Nutritional status on admission—fair.
‡Nutritional status on admission—poor.
**Nutritional status on discharge—good.
††Nutritional status on discharge—fair.
‡‡Nutritional status on discharge—poor.

§Fever: 0, Afebrile; 1, temperature up to 101 degrees for less than 1 week; 2, temperature up to 102 degrees for more than 2 days but less than 1 week; 3, temperature up to 103 degrees for 1 to 2 weeks; 4, temperature greater than 101 degrees for over 1 month.
^Fever from sulfonamide treatment.
¶Local exudation: (1) slight, (2) moderate, (3) severe, (4) very severe.

hypoalbuminemia and hyperglobulinemia with normal total plasma protein concentrations.

The *apparent* nitrogen balance was determined by comparing the total nitrogen intake from all sources with the nitrogen excretion. Nitrogen excretion was calculated by adding to the measured urinary excretion 10 per cent of the nitrogen intake to account for stool nitrogen. Loss of nitrogenous substances from the burn surface was not measured and thus could not be used in calculating nitrogen balance. *For this reason, nitrogen balance is referred to as apparent rather than true nitrogen balance.*

The *apparent* nitrogen balances of the 14 patients in this group for whom there was adequate data show that, during the first week, 6 were in *apparent* mild negative balance (1.0 to 5.0 gm. per day) while 8 were in *apparent* positive balance (1.0 to 12.0 gm. per day). By the 2d week, 12 had an *apparent* positive balance (1.0 to 14.0 gm. daily) while 2 had an *apparent* negative balance of about 2.0 grams daily. During the 3d week, only 12 of the 14 were followed. All were in *apparent*

TABLE III.—CLASS II. PATIENTS WITH SEVERE BURNS

No. Age Sex	Per cent body surface burned Total	Per cent body surface burned 3d degree	Chronic alcoholism	Complications: Fever§	Complications: Local exudation¶	Complications: Anemia	Complications: Liver disease	Diet: Time (weeks)	Diet: Average calories	Diet: Daily food intake: Protein (grams)	Diet: Daily food intake: Nitrogen (grams)	Nitrogen excretion: Time (weeks)	Nitrogen excretion: Average daily urinary nitrogen (grams)	Plasma protein concentration gm./100 ml.	Discharge day	Result
19* 26 M	15	10	0	3	3	+	+	1	1400	70	11	1	19	See Chart 5	130**	Lived
								2	1800	110	18	2	16			
								3–10	2200	125	20	3	10			
								10+	3700	156	24					
20* 37 F	15	10	0	3	2	+	0	1	1200	60	10	1	—	Remained normal with slight rise in globulin and fall in albumin	136**	Lived
								2	2200	120	19	2	8.5			
								3+	4500	180	29	3	8.5			
												4	8.5			
21* 28 F	20	10	0	2	2	0	0	1	1400	70	11	1		Remained above 5.0 and with A.+G. normal	120††	Lived
								2	2500	120	119	2				
								3+	3200	130	21	3				
22* 30 F	30	15	0	3	2	+	0	1	1400	70	11			Normal to 5th week falling to 3.6 at 8th week (A. 1.3, G. 2.3); rose to normal by 20th week	200**	Lived
								2	3000	125	20					
								3+	3500	140	22					
23* 17 F	30	15	0	3	2	+	0	1	1400	70	11			Remained above 5.0	78††	Lived
								2	2000	100	16					
								3+	3000	120	19					
24* 6 M	25	20	0	2	3	+	0	1	1800	90	14.4	1	21	Total fell to 4.8 during 1st week. A./9, G. 2.9. Then rose to 5.8 by 6th week (A. 2.3, G. 3.6)	46††	Died
								2	3500	200	32	2	21			
								3+	5000	300+	48	3	26			
												Sub.	12			
25* 10 M	30	20	0	3	2	+	0	1	1200	60	9.6	1	15	Normal in 1st 3 weeks. No further data	28††	Died (at another hospital)
								2	2000	100	16	2	20			
								3	3000	125	20	3	11.5			
26* 22 F	30	20	0	4	3	+	0	1	1200	60	9.6	1	14	See Chart 2	157‡‡	Died
								2	1500	80	12.8	2	8.5			
								3+	2000	100	16	3	8			
27* 22 M	55	45	0	4	4	+	0	1	1200	60	9.6	1	30	See Chart 3	363††	Lived
								2– 3	1850	60	14.4	2	19			
								4– 7	2000	100	16	3	18			
								8–12	2500	130	20.8	Sub.	12			
								12–26	5000	280	45					
28‡ 75 M	15	10	0	1	1	0	0	1+	4500	200	32			Total remained normal with gradual fall in A. to 2.4 and rise in G. to 3.7	26††	Died
								2								
								3								

*Nutritional status on admission—good.
†Nutritional status on admission—fair.
‡Nutritional status on admission—poor.
**Nutritional status on discharge—good.
††Nutritional status on discharge—fair.
‡‡Nutritional status on discharge—poor.

§Fever: 0, Afebrile; 1, temperature up to 101 degrees for less than 1 week; 2, temperature up to 102 degrees for more than 2 days but less than 1 week; 3, temperature up to 103 degrees for 1 to 2 weeks; 4, temperature greater than 101 degrees for over 1 month.
¶Local exudation: (1) slight, (2) moderate, (3) severe, (4) very severe.

TABLE III.—CLASS II. PATIENTS WITH SEVERE BURNS—Continued

No. Age Sex	Per cent body surface burned Total	3d degree	Chronic alcoholism	Complications: Fever§	Local exudation¶	Anemia	Liver disease	Diet: Time (weeks)	Average calories	Daily food intake: Protein (grams)	Nitrogen (grams)	Nitrogen excretion: Time (weeks)	Average daily urinary nitrogen (grams)	Plasma protein concentration gm./100 ml.	Discharge day	Result
29‡ 40 M	20	15	+	4	3	+	+	1	1200	60	9.6	1	14	See Chart 4	130††	Lived
								2– 6	1800	60	14.4	2	13			
								7– 8	5300	350	56	3	12			
								9–25	4000	200	32	Sub.	8–10			
30† 34 M	30	20	+	2	3	+	+	1	1400	70	11			Varied between 4.3 and 5.7 with A. 1.7 to 2.1, and G. 2.6 to 3.6	81‡‡	Died
								2	2500	125	20					
								3	3500	140	22					
31‡ 50 M	55	45	+	3	4	+	0	1	1200	60	9.6	1	24	Total remained normal with gradual rise in G. to 3.6 and fall of A. to 2.0	33‡‡	Died
								2	1800	100	16	2	14			
								3	2500	150	24	3	16			
								4	1500	80	12.8	Sub.	14			
32† 32 F	65	55	+	3	4	+	+	1	1200	60	14			Total gradually fell to 3.1 (A. 2.9, and G. 0.2)	27‡‡	Died
								2	1400	70	15					
								3	1800	90	13					
								4	1400	70	12					

*Nutritional status on admission—good.
†Nutritional status on admission—fair.
‡Nutritional status on admission—poor.
**Nutritional status on discharge—good.
††Nutritional status on discharge—fair.
‡‡Nutritional status on discharge—poor.

§Fever: 0, Afebrile; 1, temperature up to 101 degrees for less than 1 week; 2, temperature up to 102 degrees for more than 2 days but less than 1 week; 3, temperature up to 103 degrees for 1 to 2 weeks; 4, temperature greater than 101 degrees for over 1 month.
¶Local exudation: (1) slight, (2) moderate, (3) severe, (4) very severe.

positive balance of from 1.0 to 12.0 grams per day. Healing of the second degree areas was uncomplicated. The granulations in the third degree areas appeared pink and healthy and grafts took satisfactorily. All the patients in this class of small burns in well nourished patients lived. Fourteen of the 15 maintained their weight and were in good nutritional status on discharge. The remaining patient (Case 15), who was the most severely burned in this group, showed moderate loss of weight. The length of the hospital admissions was from 17 to 197 days.

There were 3 patients with moderate burns who were in *poor nutritional status* on entry. Two of these (Cases 16 and 17) suffered from chronic alcoholism in addition. Neither had evidence of cirrhosis. Their food intake averaged 150 to 160 grams of protein with 3,500 to 4,000 calories after the 1st and 2d weeks, respectively. Until then their food intake had been 60 to 90 grams of protein and 1200 to 2000 calories daily. Daily urinary nitrogen excretion was studied in patient 16 and was within normal limits. During the first week he was in *apparent* negative nitrogen balance and in the subsequent 2 weeks in *apparent* positive balance of about 12 grams of nitrogen per day. Neither patient developed hypoproteinemia. Both gained weight. The granulations of the third degree areas were firm and pink, and grafting was completely successful. On discharge both were in much better nutritional status than upon admission.

The third patient (Case 18) was a senile woman of 75 years, who on admission was almost cachectic. She had a poor appetite and would take almost nothing by mouth. Therefore, she was fed by stomach tube a mixture of milk and sugar amounting to 90 grams of protein and 1,700 calories per day. This was an insufficient food intake but when more food was given, gastrointestinal disturbances, especially distention and diarrhea, became distressing symptoms. However, she did not appear to lose much weight and seemed to be

making reasonable progress toward recovery when she died, after a very short illness, of bronchopneumonia.

Class II. Severe burns. In the group of 14 patients with severe burns, metabolic and nutritional disturbances were frequent and severe. The patients who were in *good nutritional status* on admission to the hospital will be considered first.

Food intake during the first week was low—60 to 90 grams of protein and 1,200 to 1,800 calories daily. Their appetites improved during the 2d week, and by the 3d week all but 3 (Cases 25, 26, and 27) were receiving from 140 to 300 grams of protein and 2,200 to 5,000 calories daily. Patient 25 was a boy of 19 years who was delirious. His appetite was not good and it was only with considerable coaxing that he ate a diet of 100 to 125 grams of protein and 2,000 to 3,000 calories. He was transferred at the end of 3 weeks to another hospital and died at the end of the 4th week. The diets of patients 26 and 27 are discussed in detail in the case report section. In short, patient 26 was a girl, aged 22 years, whose appetite was only fair. She refused supplementary feedings by tube or by vein. Her food intake was about 100 grams of protein and 2,000 calories daily. Patient 27, a male, aged 22 years, took up to 100 grams of protein and 2,000 calories daily during the first 7 weeks, and then 130 grams of protein and 2,500 calories daily for the next 5 weeks. Thereafter, his intake was raised to 300 grams of protein and 5,000 calories daily by means of gavage and intravenous supplements.

In contrast to the patients in Group I, there was definite evidence of increased urinary nitrogen excretion in many of these patients with more severe burns. Thus, of 5 in whom such measurements were made, 2 (Cases 24 and 27) excreted greater than 20 grams per day, 2 (Cases 19 and 25) between 15 and 20 grams, and 1 (Case 26) between 12 and 15 grams, while none excreted less than 12 grams daily during the 1st week. Thereafter, the urinary nitrogen excretion fell so that during the 3d week, of the 6 patients followed, 4 (Cases 19, 20, 25, and 26) excreted less than 12 grams per day, while 2 (Cases 24 and 27) continued to excrete more than 15 grams per day. After the 3d week the urinary nitrogen excretion was normal.

Considering the low food intake and excessive nitrogen excretion during the first weeks, it is not surprising to find that the *apparent* nitrogen balances in these patients were all negative in amounts from 4.0 grams to 21.0 grams per day during this time. However, by the 3d week, as the food intake was increased and the nitrogen excretion fell off, 5 of the 6 patients were in *apparent* positive balance (8.0 gm. to 18.0 gm. per day) and only one (Case 27) was still in *apparent* negative balance (4.0 gm. per day). Thereafter, the 3 patients (Cases 20, 24, and 27) followed were in *apparent* positive nitrogen balance.

All patients in this group lost weight early in the course of their illness. However, in the 5 patients with the less severe burns, the weight loss was moderate and was not progressive (see Figs. 12 to 17). In 3 (Cases 20, 21, and 23) the plasma protein concentration remained essentially normal. The other 2 showed significant plasma protein changes. Patient 22 had a normal plasma protein concentration until the 5th week when there began a gradual decline to a level of 3.6 grams per 100 milliliters by the 8th week. However, the plasma proteins rose above 4.5 grams per 100 milliliters within the next week and were normal by the 20th week after injury. Patient 19 (whose course is detailed in the case report section) had a normal plasma protein concentration until the onset of jaundice in the 11th week. At this time the plasma albumin fell to 2.0 grams per 100 milliliters, while the globulin remained at a level of 2.3 grams per 100 milliliters. In the next 3 weeks, with the regression of the jaundice, there was a gradual return of the albumin fraction to normal.

These 5 patients lived. Although they were still somewhat under weight on discharge, their general nutritional status was good. The third degree areas had been grafted without difficulty, the granulations having been firm and healthy in appearance.

Patient 25 was followed for only 3 weeks. During this time his plasma proteins remained normal and weight loss was only moderate.

The remaining 3 patients in this group (Cases 24, 26, and 27) who had the most ex-

tensive third degree burns, exhibited the most marked nutritional disturbances. The courses of 2 (Cases 26 and 27) are detailed in the case report section. In these 2, weight loss was extreme, and there was a progressive fall in the plasma protein concentration. The granulations in the third dgeree areas were soggy, edematous, and friable and there was considerably more exudate than from normal granulations. Patient 26 refused supplementary feedings, continued to lose weight, and died of malnutrition and infection on the 157th day. In contrast, patient 27 responded to a very high protein and caloric intake, with a gain in weight and loss of edema, so that skin grafting could be done. He was discharged on the 363d day. Patient 24 lost a moderate amount of weight in the first 2 weeks, but thereafter on a diet of above 300 grams of protein and 3,000 calories daily weight was maintained. His plasma protein concentration fell to 4.8 grams per 100 milliliters during the first week, but rose to 5.8 by the 6th week. The albumin concentration at this time was 2.3 and the globulin 3.6. Although sloughing of the dead tissue in the third degree areas was complete by the 4th week, there was no granulation tissue. The patient appeared to be doing fairly well when he developed an acute fulminating pyelonephritis and died on the 46th day.

Since the patients in this group were in *apparent positive nitrogen balance* during most of their course and at the same time lost weight roughly in proportion to the extent of third degree burns, it is clear that the surface loss of protein was important. As an example, patient 27 was in *apparent* cumulative positive nitrogen balance of about 1.3 kilograms at the 18th week following the burn. His weight, nevertheless, was 55 pounds below his admission weight.

There were 5 patients with severe burns who were in inadequate nutritional status on entry. Patient 31, 50 years of age, a chronic alcoholic, had a 45 per cent third degree burn. His intake varied from 60 to 150 grams of protein daily and 1,200 to 2,500 calories. Urinary nitrogen excretion was 24.0 grams daily during the 1st week, and 14.0 to 16.0 grams thereafter. He lost considerable weight, his plasma albumin fell, and the granulating third degree areas were soggy and friable. He died on the 33d hospital day, the precipitating cause being bronchopneumonia.

Patient 32, a woman of 32 years, also with chronic alcoholism, had third degree burns of 55 per cent of her body surface, and had a course similar to that described for patient 31. Fever was high and prolonged. By the 7th day her hemoglobin had fallen to 45 per cent, and thereafter frequent blood transfusions were required to keep her hemoglobin about 70 per cent. Her food intake was 60 to 90 grams of protein and 1,200 to 1,800 calories daily. Urinary nitrogen excretion was 14 to 15 grams daily for the first 2 weeks, 12 to 13 grams daily thereafter. She lost considerable weight, the plasma protein concentration fell slowly to 3.1 grams per 100 milliliters. There was marked exudation from the third degree areas, the granulations being soft and friable. During the 4th week she became slightly jaundiced and died on the 27th hospital day of bronchopneumonia.

Patient 30, a bartender, 34 years of age, also admitted to a considerable alcoholic intake. He was markedly overweight (350 pounds). He had third degree burns of 20 per cent of his body surface, and an additional 10 per cent involved with second degree burns. His food intake during the 1st week was about 70 grams of protein and 1,400 calories daily, but by the 3d week it had risen to 140 grams of protein and 3,500 calories daily at about which level it remained. Plasma protein concentration varied between 4.3 and 5.7 grams per 100 milliliters, with the albumin fraction being between 1.7 and 2.1 grams, and the globulin fraction 2.6 to 3.6 grams. His icteric index was normal throughout. Repeated blood transfusions were required to keep the hemoglobin at a satisfactory level. His temperature was about 101 degrees during most of his admission and there was moderate exudation from the third degree areas. There was no peripheral edema, and the granulation tissue appeared firm. He appeared to be doing fairly well although it was clear that he had lost a considerable amount of weight, until the 11th week when he suddenly developed bronchopneumonia and died. At autopsy a firm,

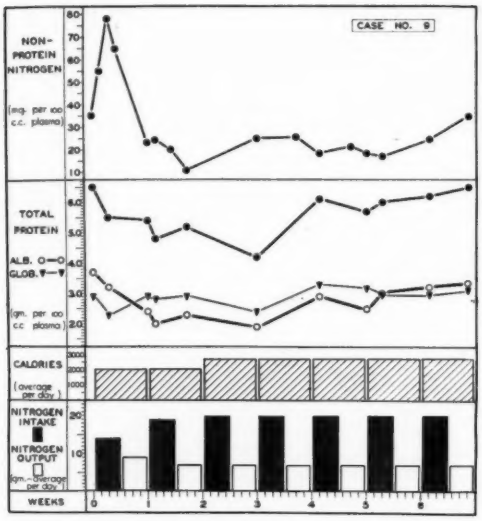


Chart 1. Note: The caloric and nitrogen intake data were averaged after the second week.

fatty liver weighing 6 kilograms was found, and he had lost 80 pounds since admission.

Patient 28, a poorly nourished man of 75 years, had a third degree burn of 10 per cent of his body surface and an additional 5 per cent of second degree burn. He was too weak to eat voluntarily; therefore, tube feeding was instituted on the 2d hospital day. His intake was about 200 grams of protein and 4,500 calories daily. He tolerated this very well and there were no gastrointestinal upsets. Fever was of low grade, and exudation from the third degree areas was slight. There was no fall in hemoglobin concentration. His total plasma protein concentration remained above 6 grams per 100 milliliters but the albumin fraction fell to 2.4 grams, while the globulin fraction rose to 3.7 grams. His weight was maintained. During the 3d week he developed urinary retention and was placed on constant drainage. His blood nonprotein nitrogen, which had been normal on entry, rose to 80 milligrams per 100 milliliters on the 21st day. During the 4th week he developed uncontrollable hiccoughing, became exhausted, and died on the 26th hospital day. At autopsy he showed a fulminating pyelonephritis as well as bronchopneumonia.

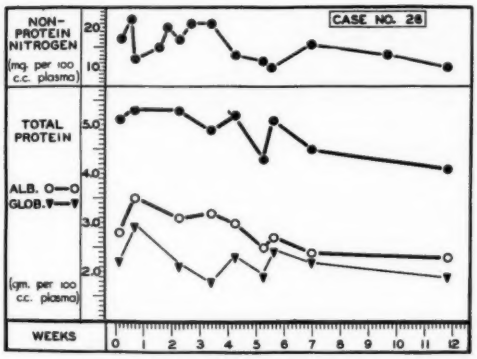


Chart 2. Data in Case 26.

The course of patient 29 is detailed in the case report section. In brief, he was 40 years old, a chronic alcoholic, with 15 per cent third degree burn; his intake for the first 6 weeks varied from 60 to 90 grams of protein, and 1,200 to 1,800 calories daily. During this time he lost weight, his plasma proteins fell to 3.9 grams per 100 milliliters, generalized peripheral edema developed, and there was considerable exudation from the edematous granulations. Thereafter, his intake was increased to 200 to 350 grams of protein, and 4,000 to 5,000 calories daily. On this regimen he gained weight, the plasma proteins rose, the edema disappeared, and grafting was successfully carried out. He was discharged on the 130th hospital day.

CASE REPORTS

The following case illustrates the course of a moderately burned, previously well nourished individual, who was kept in good nutritional status without difficulty on an oral intake of about 125 grams of protein and 2700 calories daily.

Case 9 (See Chart 1). A white woman 67 years of age was burned shortly before admission to the hospital when she was trapped in a burning house. Examination revealed a well developed and well nourished elderly woman with second and third degree burns of her head, neck, and arms. The total area of body surface involved was 15 per cent, the third degree area being 3 per cent. Local treatment consisted of the application of bentonite dressings. There was no shock. No plasma was given.

Early complications were transient oliguria and azotemia. Cystitis was present on entry and re-

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. Case 26, 13 days after injury Edema following face burn subsided. Note well nourished appearance.

Fig. 2. Case 26, hands and arms taken 46 days after injury. Note edematous pale granulation tissue.

Fig. 3. Case 26, 125 days after injury. Note the obvious loss of weight. (Compare with Fig. 1.)

sponded slowly to systemic sulfadiazine. A later complication was deep thrombophlebitis of the left leg. Her temperature ranged between 100 and 102 degrees F. for the first 3 weeks. It then came down gradually and was normal after the 5th week.

By the end of the 1st week her hemoglobin had fallen to 65 per cent. There was no specific response to iron but gradually, without transfusions, the hemoglobin rose to 70 to 75 per cent.

Her appetite was only fair during the 1st week; her daily intake averaged about 90 grams of protein and 2,000 calories. Thereafter, her appetite improved so that she was taking about 125 grams of protein and 2,700 calories daily. There were no gastrointestinal disturbances. Her daily urinary nitrogen excretion averaged 9 grams during the first week, and about 7.0 grams thereafter. She was, therefore, in *apparent positive nitrogen balance* throughout her course. Transient hypoproteinemia due to lowering of the albumin fraction was present during the 2d and 3d weeks. Thereafter, the albumin gradually rose, reaching a normal level at the 5th week.

The second degree areas were healed by the 16th day. There was only moderate exudate from the third degree areas, and the granulations were firm and pink. These areas were grafted, and the patient was discharged on the 80th hospital day in good health, having maintained her weight throughout her course.

The following patient's course illustrates the development of progressive malnutrition in a severely burned, previously healthy young girl, in whom supplementary measures to maintain her nutrition were refused.

CASE 26 (See Chart 2 and Figs. 1 to 3). A white girl aged 22 years, with an irrelevant past history, was burned in the Cocoanut Grove fire, suffering third degree burns of 20 per cent of her body surface, with an additional 10 per cent involved in second degree burns. Examination on admission revealed a healthy, well nourished girl in moderately severe shock. This condition responded to the infusion of plasma, the patient receiving 4.0 liters in the first 24 hours. The burned areas were treated with tannic acid and silver nitrate solutions.

During the 1st week, her temperature, which had been normal on entry, rose progressively to 103 degrees F. By the end of the 2d week her temperature had fallen to 101 degrees F. where it remained for the next 4 months. During the 5th month, her temperature varied between 101 and 102 degrees F.

Early in her course, the patient and her family became discouraged at the extent of her burns, and especially at the severity of the burns of her hands. Except for an occasional transfusion, supplementary measures, such as tube or parenteral feeding, were not permitted.

The patient's hemoglobin, which had been normal on entry, fell to 62 per cent by the 3d day, and during the next few months the hemoglobin level was kept between 60 and 70 per cent by occasional transfusions. Thereafter, all blood transfusions were refused and the hemoglobin gradually fell, reaching a level of 39 per cent at the end of the 5th month.

Her appetite was poor during the 1st week, her intake averaging 60 grams of protein and 1,200 calories daily. Thereafter, her appetite gradually improved so that by the third week (and thereafter) she took about 100 grams of protein and 2,000 calories daily. There were no gastrointestinal disorders. The urinary nitrogen excretion during the 1st week averaged 14 grams daily. During the 2d and 3d weeks it averaged 8.5 grams daily. No data are available thereafter. The plasma protein concentration gradually fell from a normal value on entry to 4.2 grams per 100 milliliters by the 5th week, at about which level it remained. In this instance both the albumin and globulin fractions were lowered. It was apparent that the patient was losing weight. The granulations were soggy, edematous,

Figs. 4 and 5. Case 27, 14 and 20 days after burn. Note extent of injury and good nutritional state.

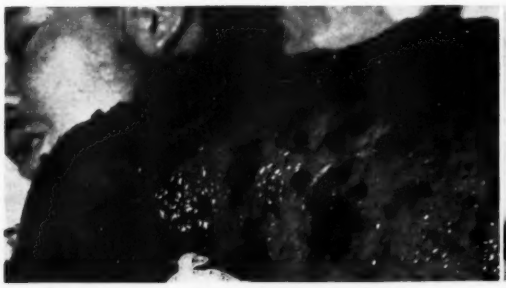


Fig. 6. Case 27, 44 days after burn. Note drawn expression of the face and edema of granulation tissue.

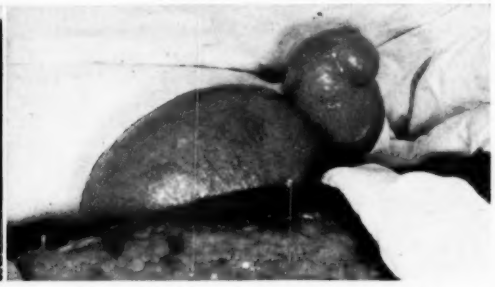


Fig. 7. Case 27, 107 days after burn. Note increased edema of granulation tissue and marked edema of genitalia.

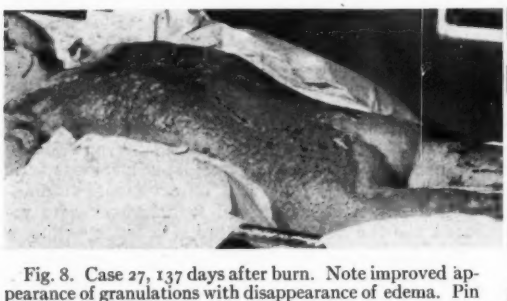


Fig. 8. Case 27, 137 days after burn. Note improved appearance of granulations with disappearance of edema. Pin point grafting begun.

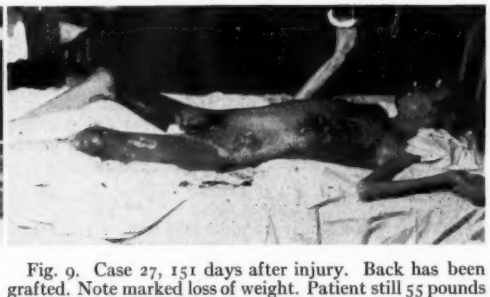


Fig. 9. Case 27, 151 days after injury. Back has been grafted. Note marked loss of weight. Patient still 55 pounds below entry weight. Large decubitus ulcer over left femur.

and friable. The exudation from these areas was excessive, considerably more than is ordinarily seen.

Weight loss continued and the patient's general condition gradually deteriorated. She developed many large and deep decubitus ulcers, and finally died of malnutrition and infection on the 158th hospital day.

In striking contrast to the preceding case are the following 2 cases in which it was possible by supplementary tube and intravenous feedings to stop, and finally to reverse, the earlier progressive weight loss and hypoproteinemia. One of these was a previously well nourished young man, the other a previously poorly nourished middle-aged man who also had chronic alcoholism. This latter patient also illustrates the development of jaundice late in the course of his illness.

CASE 27 (See Chart 3 and Figs. 4 to 11). A preliminary report of this patient has been made elsewhere (4) but is presented here in more detail. A

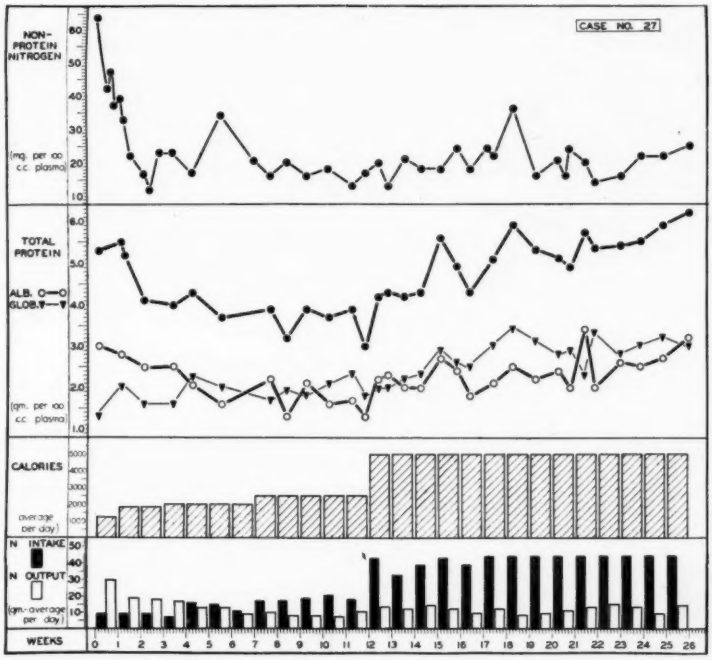
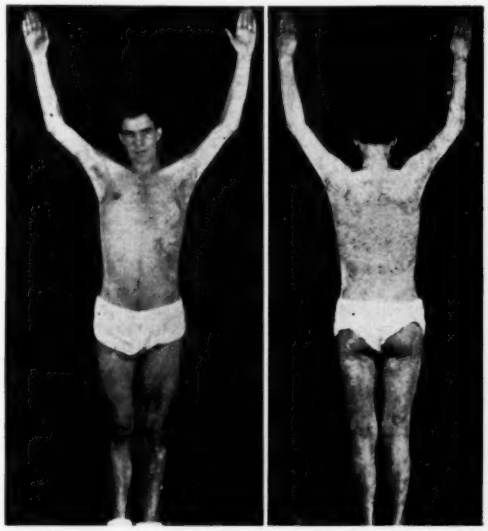


Chart 3. Note: The caloric intake data were averaged after the 12th week and nitrogen after the 17th week.

22 year old member of the United States Coast Guard, with an irrelevant past history, was in excellent health and nutrition at the time of the Cocoanut Grove fire where he sustained burns totaling 55 per cent of the body surface, with 45 per cent of the surface area involved in a third degree burn. The burns were treated with triple dye. Early hemoconcentration and shock were controlled with the infusion of 4.3 liters of plasma. Hemoglobinemia and hemoglobinuria were present during the 1st week; azotemia and oliguria for the first 2 days.

During the first 7 weeks, his temperature varied between 100 and 102 degrees F. The burns became infected by the end of the 2d week and from this time on there was a considerable amount of surface exudate. However, there was no spreading infection.

His appetite was poor during the first 4 weeks so that his daily protein intake averaged 60 grams. The daily caloric intake during the first week averaged 1,200, and rose to between 1,800 to 2,000 during the 2d to 4th weeks. During the next month, with constant urging, his intake rose to 100 grams of protein, the caloric intake remaining at about 2,000. His average daily urinary nitrogen excretion fell steadily from the high level of 30 grams during the 1st week to about 14 grams at the 5th week. During this time the plasma protein, which had been normal on admission, gradually fell to 4.0 grams per 100 milli-



Figs. 10 and 11. Case 27, 13 months after injury. All areas grafted and healed. Patient regained considerable weight but still 20 pounds below admission weight.

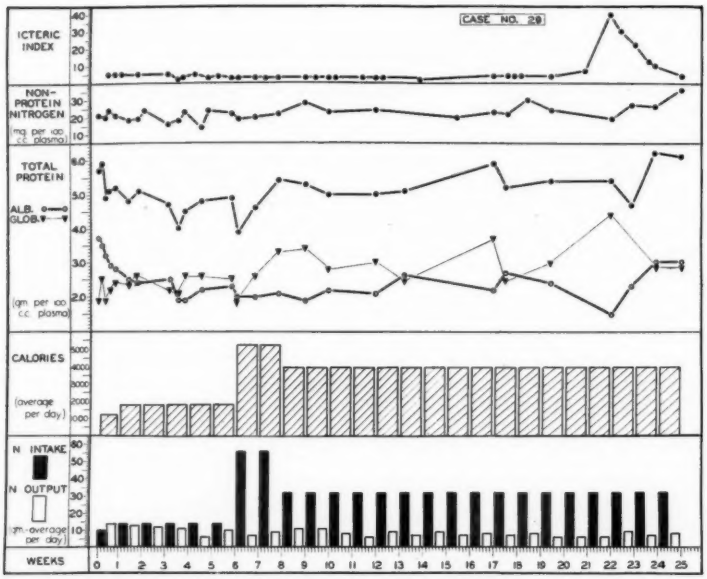

CASE NO. 29
ICTERIC INDEX
NON-PROTEIN NITROGEN
(mg. per 100 c.c. plasma)
TOTAL PROTEIN
ALB.
GLOB.
(gm. per 100 c.c. plasma)
CALORIES
(average per day)
N INTAKE
N OUTPUT
(gm. average per day)
WEEKS
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25

Chart 4. Note: The caloric and nitrogen intake data were averaged after the 7th week.

liters at the end of the 6th week. This fall was due almost entirely to a fall in the albumin fraction. Clinically, the patient had lost considerable weight and at the end of the 5th week edema became evident and increased progressively.

At the end of the 7th week his appetite improved somewhat so that his food intake rose to 130 grams of protein and 2,500 calories daily. Despite this, his plasma protein continued to fall, reaching the low level of 3.0 grams per 100 milliliters at the 12th week, the albumin concentration having fallen to 1.2 grams per 100 milliliters. His peripheral edema continued to increase. The granulation tissue was soggy and the exudate from the burned surfaces increased progressively.

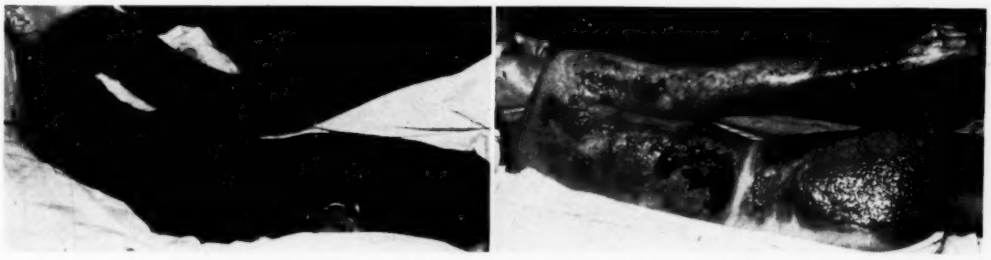
At this time tube and intravenous supplements were begun. Albumin, concentrated plasma, and casein hydrolysate were used for the parenteral feedings. By these means his intake was raised to 275 to 300 grams of protein and 5,000 calories daily. There were no gastrointestinal disorders. Urinary nitrogen excretion did not rise but remained about 14 grams daily. The plasma albumin rose within a week to 2.4 grams per 100 milliliters, the globulin still remaining at 1.8 grams. Following this, the globulin rose, reaching a level of 3.4 grams at the end of the 18th week. The albumin during this time had risen more slowly, being only 2.6 grams. Hippuric acid, cephalin flocculation, and prothrombin tests were within normal limits at this time.

Coincident with the rise in plasma proteins was a striking decrease in edema. The granulations became firm and the amount of exudate decreased. Considering the factors of decreasing surface exudation, stationary urinary nitrogen excretion, and normal gastrointestinal function, together with the markedly increased intake, it is clear that his nitrogen balance during this period was markedly positive. This would indicate a pre-existing protein deficit of considerable magnitude, in spite of the previously *apparent positive nitrogen balance.* This was borne out by the fact that his weight at this time, even after an obvious gain in weight and strength, was still 55 pounds below his admission weight.

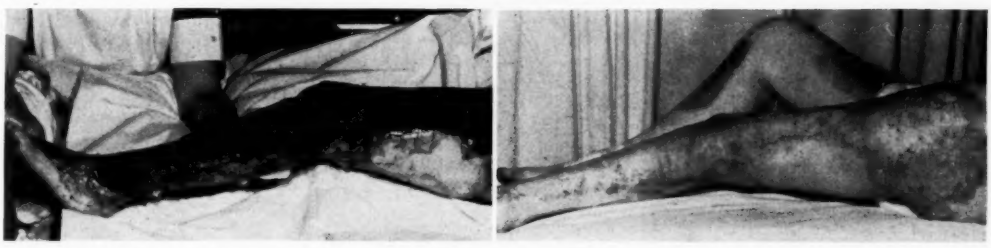
His general condition had improved considerably and skin grafting, hitherto impossible because of the patient's debilitated state and edematous granulations, was begun. All areas were covered with skin by the 32d week. During this time his appetite had improved so that he was able to take about 280 grams of protein and 5,000 calories daily by mouth. Supplementary feedings were omitted. He continued to gain weight at the rate of 1¼ pounds per week, and was discharged in good health 1 year after the burn.

CASE 29 (See Chart 4). A 40 year old male, chronic alcoholic, was burned by flaming kerosene shortly before entry. Fifteen per cent of his body surface was involved in third degree burns, with an additional 5 per cent involved by second degree burns. He was markedly under weight on admission and admitted to a very poor dietary intake. Mild shock, responding to the administration of 1.0 liter

Figs. 12 and 13. Case 22, 38 and 82 days after injury. Note maintenance of weight and good nutrition in a patient with a severe burn.



Figs. 14 and 15. Case 21, 13 and 59 days after injury. Note maintenance of good nutrition and healthy firm granulation tissue.



Figs. 16 and 17. Case 29, 17 and 143 days after injury. Note size of leg shortly after admission and on discharge is about the same, indicating maintenance of patient's weight and nutrition.

of plasma, was present in the first 12 hours. Petrolatum gauze pressure dressings were applied to the burned areas.

His hemoglobin, which had been normal on entry, fell to 60 per cent by the end of the 3d week. Thereafter, frequent transfusions were required to keep the hemoglobin between 70 and 85 per cent.

During the first 6 weeks the patient was maintained on the routine house diet and took about 90 grams of protein and 1800 calories daily. The daily urinary nitrogen excretion averaged 14 grams during the first week. Thereafter it gradually fell, reaching a level of 9 grams per day by the 6th week, at about which level it remained throughout the rest of his course.

Plasma protein concentration, which had been normal on entry, fell to 4.7 grams per 100 milliliters by the 3d week. In the next 3 weeks it fell still fur-

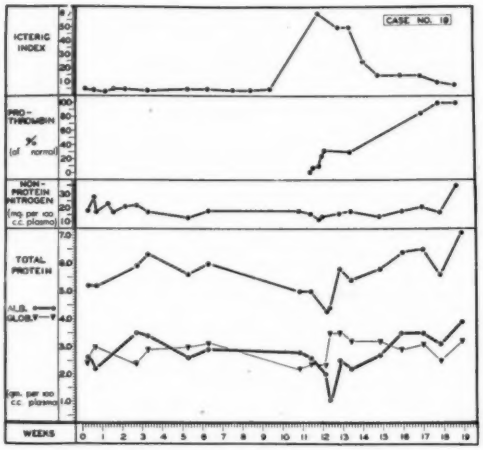


Chart 5. Data in Case 19.

ther, to 3.9 grams. The albumin level at this time was 2.0 grams, the globulin 1.9 grams. Thus, the drop in total plasma protein concentration was chiefly the result of a progressive fall in the albumin fraction. Minimal peripheral edema was present. The third degree areas were free of slough but there was considerable exudate from the granulations which were soggy and friable.

Marked weight loss was evident by this time. Measures were taken to increase his food intake to about 230 grams of protein and 4,200 calories daily. In addition, he was given 120 grams of casein hydrolysate and 100 grams of dextrose, intravenously daily for the next 2 weeks.

The urinary nitrogen excretion did not increase but remained at 10 grams per day. No diarrhea or other gastrointestinal disturbances developed. The exudate from the granulating areas decreased. His *apparent nitrogen balance* became positive by approximately 50 grams per day. As in the case of the preceding patient, this indicated a pre-existing protein deficit of considerable magnitude. During this time the plasma globulin rose, reaching a level of 3.5 grams at the 9th week. The albumin fraction lagged behind, beginning to rise only at the 12th week. At this time the globulin fraction began to fall so that in 1 week the albumin and globulin fractions were equal. Edema disappeared and there was a slow but definite gain in weight. His temperature, which had been elevated to 100 to 103 degrees F., became normal. Granulations became firm and pink and skin grafting was carried out successfully.

During the 22d week, the patient began to complain of nausea and mild postprandial epigastric distress. Slight jaundice appeared, the icteric index gradually rising to 40 units. Bile was present in the urine. At no time was there increased urobilinogen in the urine. The hippuric acid excretion was 0.7 gram. Cephalin flocculation was one plus. Neither the liver nor spleen became palpable. Total white blood cell counts were about 5,000 per cubic millimeter. The patient was afebrile during this episode.

No special therapeutic measures were taken. During the next week the gastrointestinal disturbances disappeared, and, in the next 2 weeks the icteric index, hippuric acid and cephalin flocculation tests returned to normal. His course thereafter was uncomplicated and he was discharged in good health on the 130th day.

The following case also illustrates the development of late jaundice, in this instance in the course of a previously healthy, well nourished young male with severe burns.

CASE 19 (Chart 5). A 26 year old white male received third degree burns of 10 per cent and second degree burns of 5 per cent of his body surface at the Cocoanut Grove fire. Moderately severe shock present in the first 12 hours responded to plasma infusions. During the first 24 hours he was given 3.5 liters of plasma. The burned areas were treated with triple dye.

His temperature rose to 104 degrees F. the first day but fell to 100 degrees F. on the following day. Thereafter, it varied between 99 and 100 degrees F.

During the first 5 days his hemoglobin fell from a normal value on admission to 60 per cent. Frequent transfusions were required thereafter to maintain his hemoglobin above 70 per cent.

During the first week his appetite was poor and his food intake was about 70 grams of protein and 1,400 calories daily. Thereafter, his appetite improved somewhat so he was taking about 125 grams of protein and 2,200 calories daily. There were no gastrointestinal disorders at this time. He was receiving as vitamin supplements only thiamin and vitamin C. The urinary nitrogen excretion during the first week was elevated, averaging 19 grams daily. During the 2d week it averaged 16 grams daily and thereafter it was about 10 grams per day. There was a fairly large amount of exudate from the burned surfaces, so that despite the *apparent positive nitrogen balance* he was actually becoming protein deficient. This was evidenced by a moderate loss of weight. Plasma proteins remained normal during this period.

During the 11th week he complained of vague postprandial epigastric distress and a few days later became jaundiced. There was no hemoglobinemia. The stools were for a few days almost clay-colored, but bile was present in one specimen of urine. More complete oral and parenteral vitamin supplements were begun at this time. There was a striking increase in his appetite so he was able to take 150 grams of protein and 3,700 calories daily. There began a slow but definite gain in weight. At the height of his jaundice (icteric index 60, on the 83d day), the prothrombin concentration was less than 1 per cent of normal. In spite of 10 milligrams of a preparation of 2

methyl-1, 4-naphthoquinone intravenously daily for 3 days, the prothrombin time did not return to normal for about 6 weeks. During this time the icteric index had fallen to 10. The white blood cell counts were about 7,000 per cubic millimeters. During this same period his total plasma protein concentration fell to a level of 4.3 grams per 100 milliliters due to a drop in the albumin fraction to 1.0 grams. However, within 4 weeks the plasma proteins, hippuric acid, and cephalin flocculation tests returned to normal. The liver and spleen were never palpable, and he was afebrile throughout this episode. The amount of surface exudate decreased and grafting of the third degree areas was carried out. His further course was uncomplicated, and he was discharged in good health on the 130th day.

OBSERVATIONS

The difficulties encountered in the nutritional care of the burned patients are due to the coexistence, in one individual, of several factors, each of which is capable of causing an increased demand for food. It has been previously stated by other authors (24, 28) and by preliminary studies from this hospital (40, 42, 43) that the principal demand of the burned individual is for nitrogen. This increased nitrogen demand results chiefly from the excessive loss of nitrogen into the urine during the first few weeks and later large losses of nitrogenous material from the burned surface. It is clear from the data presented that the increased nitrogen requirement is related to the severity of the burn, particularly to the extent of third degree injury. Thus, the patients comprising Group I who had less than 7 per cent surface area of third degree burn, presented only minor nutritional problems. In general, these patients' appetites were good, urinary nitrogen excretion was normal and exudation from the burned surfaces was not excessive. On a diet of 125 grams of protein and 2,800 calories daily, there were no marked losses of weight and occasionally an actual gain in weight. The granulation tissues in the third degree areas were firm and pink, and grafts were successful. These findings are in sharp contrast to those obtained in patients with *severe burns*, presented in Group II. Here appetites were generally poor, urinary excretions of nitrogen were excessive, and there were considerable exudations from burned surfaces. Progressive loss of weight, hypoproteinemia, and edema followed.

The cause of the excessive loss of nitrogen in the urine has not been finally determined. There may be more than one precipitating factor. A certain number of the patients studied had a transitory azotemia (20). However, clearing of the increased nonprotein nitrogenous products in these patients accounted for only a small fraction of the total urinary nitrogen increase. In severely burned patients there is destruction of large amounts of tissue, probably followed by autolysis and absorption of protein breakdown products. In addition, a general increase in protein breakdown may result from the so called "toxic degeneration of protein" associated with fever and infection (33). There is also the possibility that the protein catabolism is increased by the absorption of specific substances from the burned areas (30). It may be that increased gluconeogenesis may be responsible for part of the increased protein breakdown. Browne (9) postulates an increased production of "S" hormone by the adrenal cortex and simultaneously a decreased production of "N" hormone resulting in an increased protein breakdown as a step in the formation of glucose. In any event it has been recently shown that marked abnormalities of the carbohydrate metabolism do occur in severely burned animals and humans and are associated with hyperglycemia, lactacidemia, and a lowered carbon dioxide combining power (12, 30).

In severe burns the losses of nitrogen from the burned surfaces comprise not only the loss of plasma during the first few days, but a continuous exudation of nitrogenous material from the injured tissue until such time as the surface is covered by new skin. That these losses can be very large has recently been shown by Hirshfeld and by Co Tui. Like the increased loss of nitrogen in the urine the amount lost from the burned surface varies directly with the extent and depth of the burn. In the present study the amount of surface loss was estimated but not determined. In typical second degree burns, the loss of nitrogen occurs soon after the trauma and is due chiefly to the external oozing of plasma-like fluid. This nitrogen loss usually ceases within a few days and, thereafter, in an uncompli-

cated second degree burn the nitrogen loss from the surface is minimal. In the typical third degree burn there is at first little ooze from the surface. However, after a week or so, sloughing of the dead tissue begins and from this time on the loss of nitrogenous products may be considerable. The surface loss thus becomes important at the time when the urinary nitrogen excretion has returned to normal. The importance of the loss of protein from the granulating surfaces is evidenced by the continued loss of weight, fall in plasma protein, and development of edema in some patients who were in *apparent positive nitrogen balance as regards nitrogen intake and its output in the urine.* It is clear that conventional nitrogen balance studies when applied to severely burned patients fail to show the minimal needs of the patient for protein.

Failure to meet the increased nutritional demands of the severely burned patient results in progressive loss of weight and the development of hypoproteinemia. The occurrence of progressive hypoproteinemia is an extremely serious metabolic sign. During the first week following a burn a *transitory* hypoproteinemia may well result, due to shifts of water, electrolyte, and protein from the blood stream into subcutaneous tissue or exudates. This early hypoproteinemia is without nutritional significance. Such losses of protein as have occurred may be met by suitable transfusions of plasma and the various displacements of extracellular fluid restored by suitable electrolyte therapy. On the other hand, a continuous fall in the plasma proteins after the first week is a sign of marked tissue protein deprivation. Sachar and his co-authors have stated that for each gram reduction in the total circulating plasma albumin, some 30 grams of tissue protein have already been lost. Thus, marked tissue protein deprivation *may exist in the face of a normal, or very slightly reduced, plasma protein concentration.* Unless remedial steps are taken early, weight loss continues and the plasma proteins fall progressively. Finally, edema and evidence of marked loss of weight and strength develop, and death from malnutrition ensues. This was demonstrated by the courses of patients 26, 31, and 32. In contrast, in spite of the development of severe malnutrition in patients 27 and 29, it was possible to stop, and finally to *reverse*, the weight loss and hypoproteinemia by supplying adequate nutrition by mouth, gavage, and the intravenous route. This was followed by a gradual return of these patients to health.

It is preferable to anticipate the requirements of the patient and to meet them before severe malnutrition occurs, as was done in patients 19, 20, 21, 22, 23, and 28. In the very severely burned patient this may require as much as five times the normal intake of nitrogen. It has been indicated that the principal foodstuff required by the burned individual is protein. However, the food provided must be an adequate metabolic mixture containing, in addition to adequate amounts of protein, sufficient calories, fats, carbohydrates, minerals, water and accessory food substances.

Supplying food by mouth is the most satisfactory way of maintaining nutrition, both from the sense of well-being of the patient and for the maintenance of normal gastrointestinal function. However, when the caloric and protein requirements are greatly increased the diet necessary to meet these demands often becomes unpalatable and bulky. As a result, anorexia, nausea, and often vomiting, and diarrhea may occur. Furthermore, the ingestion of food by severely burned patients is difficult because of abnormal and uncomfortable positions due to the distribution of the injury and the presence of pain. Under these circumstances supplemental feedings by gavage or infusion are necessary. If tube feeding is carried out it is well to begin cautiously, increasing the concentration and amount of the mixture gradually over a period of days in order to avoid gastrointestinal upsets. In some individuals protein hydrolysates are better tolerated than whole protein.

Casein hydrolysates and mixtures of amino acids have been shown to be an adequate source of protein (16, 35) provided the essential amino acids are supplied in the required amounts (4). Several practical difficulties in the use of casein hydrolysate and glucose intravenously in the large amounts required were encountered. Certain hydrolysates, even

after the *p*H was adjusted to neutrality, caused pain when infused and frequently sclerosis of the vein followed. This is an important consideration in the treatment of severely burned patients, since such individuals have few superficial veins available, and these must be kept open for the necessary frequent blood transfusions. Nausea and vomiting were also observed during the administration of casein hydrolysates. These occurred most frequently when the rate of injection of the material was greater than 0.5 gram per minute. As a rule, with reduction in the rate, these symptoms stopped.

In addition to increasing the protein intake, the caloric requirement must be maintained at a high level. If this is not done, protein will be broken down to supply the necessary body energy. Fat represents the most concentrated source of calories. However, excessive fat in the diet should be avoided in burned patients due to the possibility of liver disease. A large proportion of the calories required must therefore come from carbohydrates. Since there is evidence in animals (12) that the muscle carbohydrate reserves are depleted after burns, the necessity for a high carbohydrate intake may be even greater than would be required from the caloric viewpoint alone.

No studies have been made concerning vitamin requirements. However, it is probable that there is an increased demand for these accessory foodstuffs. A diminished appetite occurred frequently in the severely burned patients and was a limiting factor in the supplying of adequate food by mouth. In 1 patient (Case 19) following the addition of the vitamin supplements to the diet, there was a striking increase in appetite. However, this observation was not made on other patients. Nearly all were given five times the optimum allowances stated by the National Research Council (13) as adequate for normal individuals of vitamins A and D, ascorbic acid, thiamin, riboflavin, and niacin. In addition, 50 milligrams of pyridoxine and ca-pantothenate were given daily. Yeast and crude liver extract were administered also.

The previous state of nutrition of the patient on admission was an important factor in his subsequent course. The poorly nourished individual with diminished reserves is not equipped to withstand a prolonged period of negative balance as well as the previously well nourished individuals. Also it was often more difficult to feed the poorly nourished patients as adequately as the well nourished ones. The latter had better appetites and tolerated high protein, high caloric diets much better, while in the former the forcing of food frequently produced anorexia, nausea, vomiting, and diarrhea. Only gradually could the diet of previously malnourished patients be increased and under some circumstances it was impossible to increase it sufficiently.

There have been some differences reported between the response of well and poorly nourished people to the administration of nitrogen shortly after injury. Browne found that young, previously healthy, and well nourished patients did not retain a moderate addition of dietary protein during the early catabolic period following traumatic injury, while patients who were previously poorly nourished did retain such an increase in the protein administered. Similar results were reported by Howard in patients with fractures. No clear-cut data on this point can be gathered from the cases presented here, since no attempt was made to force the nitrogen intake in the well nourished individuals during the first week. However, all individuals could be put into apparent positive balance in the 2d week. Cope and associates have reported 2 patients, who were previously well nourished, with severe burns who were in *apparent positive nitrogen balance* during the first week following the injury. However, a major portion of the calculated protein intake was in the form of intact red cells. It is controversial whether red cell hemoglobin is actually available as part of the metabolic mixture during the period under consideration. In a recent review of this subject, Whipple states: "Hemoglobin in its production may draw on the plasma protein but hemoglobin stands apart in the protein economy and does not contribute freely to the protein pool." Studies on this point in humans are at present in progress in this laboratory. The nitrogen intake from transfused whole blood was not

included in the protein intake figures recorded in this paper.

Liver damage in patients with thermal burns occurring shortly after the injury has been reported by several investigators (5, 10, 48). The jaundice and other evidence of liver damage appeared usually within the first week and was part of the so called "toxemia of burns." Central necrosis of the liver was found at postmortem examination. Wells and his co-workers and others (2, 3, 18, 23, 45) have shown that treatment with tannic acid was a probable cause of such early liver damage. Early diminished liver function and necrosis have also been reported in patients treated with gentian violet and triple dye (21, 49), and to a lesser extent in patients treated with bland surface agents (27). None of the patients in this series showed clinical evidence of early liver damage. Three patients became jaundiced late in the course of their illness. Patient 32, who also had chronic alcoholism with very extensive third degree burns, developed severe malnutrition and infection. She became jaundiced on the 22d day and died of bronchopneumonia on the 27th day. Her burns had been treated with "triple dye." Autopsy revealed slight central necrosis of the liver.

Jaundice appeared 3 to 4 months after the burn in 2 patients (Cases 19 and 29). In both patients the jaundice was preceded by a 2 to 3 day period of epigastric distress. During the period of jaundice lasting 2 to 3 weeks, the patients were afebrile, the white counts were normal or low, the stools were light in color but not completely acholic, and bile was present in the urine. There was no hemoglobinemia and urine urobilinogen excretion was within normal limits. Sodium benzoate conjugation and prothrombin times were abnormal during the period of jaundice but became normal as the icterus disappeared. No specific therapy was instituted other than that of increasing the food and vitamin intake. The jaundice lasted 3 and 6 weeks, respectively. There was no evidence of permanent liver damage. Patient 19 was treated initially with tannic acid and silver nitrate, while patient 29 was treated with petroleum jelly pressure dressings.

There is considerable evidence that adequate nutrition, especially of protein, carbohydrate, and certain of the vitamins plays an important rôle in the prevention and treatment of liver disease (8, 32). In this connection, patient 19 was a previously well nourished young man, who had lost a moderate amount of weight during the first few months following injury. He was given only thiamin, vitamin C, and brewer's yeast as vitamin supplements during this time. In contrast, patient 29 was a 40 year old, chronic alcoholic who was in poor nutritional status on admission. Although he had lost considerable weight during the first 6 weeks following injury, his nutritional status was improving on a very high protein and caloric diet at the time of the onset of the jaundice. He had received full supplements of vitamins from the time of entry (see method). These patients had received infusions of large amounts of whole blood and blood plasma. Therefore, the possibility of "homologous serum jaundice" must also be considered (31, 37, 38).

Liver disease may antedate the injury, especially in the patients with chronic alcoholism who constitute a large proportion of the patients admitted with burns. One patient (Case 30), a bartender who had chronic alcoholism, had *persistent* hyperglobulinemia but no icterus up to his death. At autopsy a fatty liver weighing 6 kilograms was found and was thought to be of long standing. His burns had been treated with tannic acid and silver nitrate and with "triple dye."

SUMMARY

1. Thirty-two patients with burns were studied with respect to their nitrogen metabolism and their nutritional demands.

2. The nutritional disturbances observed, and especially the increased demand for protein, was found to be directly related to the extent of the third degree burn.

3. High caloric, high vitamin diets with up to 400 grams of protein per day were necessary to maintain adequate nutrition in some patients with very severe burns.

4. When this quantity of food could not be taken or tolerated, gavage and intravenous supplements were given.

5. Patients who were poorly nourished at the time of injury had less protein reserves and quite often developed gastrointestinal disturbances when given a high caloric, high protein diet.

6. In those patients whose nutritional requirements were not met, malnutrition developed, skin grafting and healing were delayed and, frequently, death ensued.

7. The importance of supplying adequate nutrition from the earliest possible moment is stressed.

8. The occurrence of late jaundice in burned patients is described and discussed.

REFERENCES

1. ALDRICH, R. H. Chapter in Mason's Pre-operative and Post-operative Treatment. Philadelphia: W. B. Saunders Co., 1938.
2. BAKER, R. D., and HANDLER, P. Ann. Surg., 1943, 118: 417.
3. BARNES, J. M., and ROSSITER, R. L. Lancet, Lond., 1943, 22: 18.
4. BASSETT, S. H., WOOD, R. R., SHULL, F. W., and MADDEN, S. C. N. England J. M., 1944, 230: 106.
5. BELT, T. H. J. Path. Bact., Lond., 1939, 48: 493.
6. BERKOW, S. G. Arch. Surg., 1924, 8: 138.
7. BRIDGES, M. A. Food and Beverage Analysis. Philadelphia: Lea & Febiger, 1935.
8. British Ministry of Health. Homologous Serum Jaundice. Lancet, Lond., 1943, 1: 83.
9. BROWNE, J. S. L. Personal communication.
10. BUIS, L. J., and HARTMAN, F. W. Am. J. Clin. Path., 1941, 11: 275.
11. CAMERON, R. F., and ALLEN, J. W. Lancet, Lond., 1943, 2: 179.
12. CLARK, E. J., and ROSSITER, R. J. Q. J. Exp. Physiol., Lond., 1944, 32: 279.
13. Committee on Foods and Nutrition, National Research Council: Recommended Dietary Allowances. Washington: Nutritional Division, Federal Security Agency, 1941.
14. COPE, O., NATHANSON, I. T., ROURKE, G. M., and WILSON, H. Ann. Surg., 1943, 117: 937.
15. CO TUI, WRIGHT, A. M., MULHOLLAND, J. H., BARCHAM, I., and BREED, E. S. Ann. Surg., 1944, 119: 815.
16. ELMAN, R. Physiol. Rev., 1944, 24: 372.
17. Idem. Proc. Soc. Exp. Biol., N. Y., 1938, 37: 610.
18. ERB, I. H., MORGAN, E. M., and FARMER, A. W. Ann. Surg., 1934, 117: 234.
19. FINLAND, M., DAVIDSON, C. S., and LEVENSON, S. M. In preparation.
20. GOODPASTOR, W. E., LEVENSON, S. M., TAGNON, H. J., and TAYLOR, F. H. L. To be published.
21. GOODPASTOR, W. E., LEVENSON, S. M., and TAYLOR, F. H. L. To be published.
22. HANGER, F. M. J. Clin. Invest., 1939, 18: 261.
23. HARTMAN, F. W., and ROMENCE, H. L. Ann. Surg., 1943, 118: 402.
24. HIRSHFELD, J. W., WILLIAMS, H. H., ABBOTT, W. F., HELLER, C. G., and PROLING, M. A. Surgery, 1944, 15: 766.
25. HOWARD, J. E. Bull. Johns Hopkins Hosp., 1944, 54: 313.
26. HOWE, P. E. J. Biol. Chem., 1921, 49: 93.
27. LEE, W. E., and RHOADS, J. E. J. Am. M. Ass., 1944, 125: 610.
28. LUCIDO, J. Ann. Surg., 1940, 111: 640.
29. MURPHY, W. P. Boston M. & S. J., 1926, 194: 297.
30. MUUS, J., and HARDENBERGH, E. J. Biol. Chem., 1944, 152: 1.
31. OLIPHANT, J. W., GILLIAM, A. G., and LARSON, C. L. Pub. Health Rep., Wash., 1943, 58: 1233.
32. PATEK, A. J., JR., and POST, J. J. Clin. Invest., 1941, 20: 481.
33. PETERS, J. P., and VAN SLYKE, D. D. Quantitative Clinical Chemistry. Interpretations. Vol. 1, p. 294. Baltimore: Williams & Wilkins, 1932.
34. QUICK, A. J. Arch. Int. M., 1936, 57: 544.
35. SACHAR, L. A., HORVITZ, A., and ELMAN, R. J. Exp. M., 1942, 75: 453.
36. SOUTER, A. W., and KARK, R. Am. J. M. Sc., 1940, 200: 603.
37. STEINER, R. E., Brit. M. J., 1944, 1: 110.
38. Ibid., 1944, 1: 105.
39. STRANGE, W. W., and MAUROT, A. J. U. S. Nav. M. Bull., 1943, 41: 953.
40. TAYLOR, F. H. L., DAVIDSON, C. S., and LEVENSON, S. M. Connecticut S. M. J., 1944, 8: 141.
41. TAYLOR, F. H. L., LEVENSON, S. M., and ADAMS, M. A. N. England J. M., 1944, 231: 437.
42. TAYLOR, F. H. L., LEVENSON, S. M., DAVIDSON, C. S., and ADAMS, M. A. N. England J. M., 1943, 229: 855.
43. TAYLOR, F. H. L., LEVENSON, S. M., DAVIDSON, C. S., BROWDER, N. C., and LUND, C. C. Ann. Surg., 1943, 118: 215.
44. TURKEL, H., and BETHELL, F. H. J. Lab. Clin. M., 1943, 28: 1246.
45. WELLS, D. B., HUMPHREY, H. D., and COLL, J. J. N. England J. M., 1942, 226: 629.
46. WHIPPLE, G. H. Am. J. M., Sc., 1942, 203: 477.
47. WILLIAMSON, C. R. Personal communication.
48. WILSON, W. C., MACGREGOR, A. R., and STEWART, C. P. Brit. J. Surg., 1938, 25: 826.
49. WOLFF, W. A., ELKINGTON, J. R., and RHOADS, J. E. Ann. Surg., 1940, 112: 158.

ABSORBABLE OXIDIZED CELLULOSE WITH THROMBIN AS A HEMOSTATIC AGENT IN SURGICAL PROCEDURES

ALFRED UIHLEIN, M.D., F.A.C.S., O. THERON CLAGETT, M.D., F.A.C.S.,
ARNOLD E. OSTERBERG, Ph.D., and WARREN A. BENNETT, M.D., Rochester, Minnesota

FOR many years the need for a relatively absorbable, nonirritating hemostatic agent in surgical procedures has stimulated interest in the development of such a substance. In 1944, Ingraham, Bailey (5), and Nulsen (6) reported effective hemostasis in neurosurgical procedures with fibrin foam, an absorbable hemostatic agent prepared from human fibrinogen and human thrombin. In 1942, Kenyon and collaborators (9, 11) in the Eastman Research Laboratories suggested that oxidized cellulose might be suitable. Recently this material was prepared and was found to have satisfactory hemostatic properties when saturated with thrombin in a saline solution (7).

Absorbable oxidized cellulose is prepared in the form of a transparent gauzelike material and a heavier material that resembles absorbent cotton. The gauze is 3 inches square and the heavier material is in a compact strip that measures ½ inch in width and 1¾ inches in length (Fig. 1). The material, placed in individual sterile envelopes, cannot be reautoclaved since it disintegrates. It may be boiled 3 minutes or kept in 70 per cent alcohol until used.

The manufacturer also supplies concentrated dried thrombin in ampules containing either 5,000 or 10,000 units. The thrombin should be dissolved in no more than 5 cubic centimeters of a sterile saline solution to avoid dilution and consequent decrease in potency. When absorbable oxidized cellulose is to be saturated with thrombin, it first should be dipped in a 1 per cent solution of sodium bicarbonate to which has been added as an antiseptic a 1:5,000 solution of phemerol (paratertiary-octylphenoxy-ethoxy-dimethyl-benzyl ammonium chloride monohydrate). This solution neutralizes the slightly acidic reaction of oxidized cellulose due to the presence of free carboxyl groups and thus prevents the neutral solution of thrombin from being inactivated. Seegers and Doub found that oxidized cellulose which contains approximately 20 per cent of carboxyl groups destroys thrombin *in vitro*. This additional precaution does not appreciably delay the immediate availability of the hemostatic agent and insures its satisfactory utilization.

In 1943, Frantz (2) reported the results of some experimental studies with oxidized cellulose in animals. She found that it was absorbed when implanted into animal tissues and that it produced little cellular reaction. It was only mildly irritating when placed on the surface of the brain. Galbraith also used absorbable oxidized cellulose as a hemostatic agent in experimental animals after soaking it in a solution of thrombin and applying it to bleeding surfaces. Cronkite found that a combination of thrombin with soluble cellulose appeared to be of value for local hemostasis in both traumatic and elective surgical procedures. Frantz and associates (3) recently completed a review of surgical cases in which absorbable cellulose was used for hemostasis.

Absorbable oxidized cellulose was made available[1] to surgeons of the Mayo Clinic for clinical trial as a hemostatic agent. The two types of material, that is, the gauzelike and cottonlike substance, had been used for 4 months at the time of preparation of this report. Accurate protocols were kept in 60 cases in which the usual methods of hemostasis had failed. The results indicated that the 2 types of absorbable oxidized cellulose were equally effective.

COMMENT

Absorbable oxidized cellulose was used in an effort to control oozing and bleeding in 22 surgical cases, 20 neurosurgical cases, 11 oto-

From the Section on Neurologic Surgery, the Division of Surgery, the Section on Clinical Biochemistry, and the Section on Neuropathology, Mayo Clinic.

Since this paper was written Dr. Uihlein has become Captain in the Medical Corps, A.U.S.

[1] By Dr. E. A. Sharp, of Parke, Davis and Company.

TABLE I.—ABSORBABLE OXIDIZED CELLULOSE WITH THROMBIN AS A HEMOSTATIC AGENT: REVIEW OF SIXTY CASES

Surgical fields	Type of material used		Degree of hemostasis			Total	
	Gauze-like	Cot-tonlike	Excel-lent	Satis-factory	Poor	Cases	Per Cent
			Cases	Cases	Cases		
General	12	10	13	8	1	22	36.7
Neurologic	5	15	12	6	2	20	33.3
Otolaryngologic	4	7	9	2	0	11	18.3
Orthopedic	4	0	1	3	0	4	6.7
Proctologic	2	1	2	1	0	3	5.0
Total	27	33	37	20	3	60	100.0
Per cent of 60 cases	45	55	62	33	5		

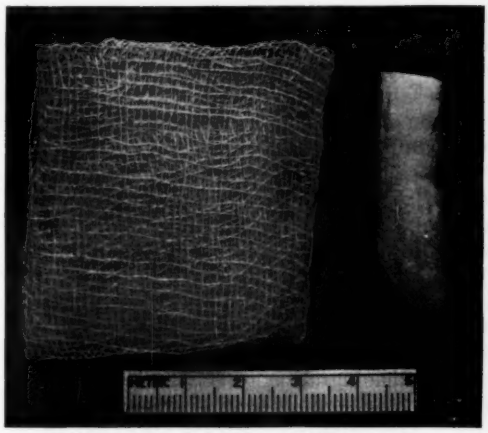


Fig. 1. Gauzelike and cottonlike material.

laryngologic cases, 4 orthopedic cases, and 3 cases in which rectal operations were undertaken. At the completion of operation, the surgeon classified the effect of the hemostatic agent as excellent, satisfactory, or poor. The final results were prepared from a review of the histories after dismissal of the patients.

Excellent immediate hemostasis was obtained in 37 cases (62 per cent) and satisfactory hemostasis in 20 cases (33 per cent) in which either the gauzelike or cottonlike material was used. In 3 cases (5 per cent) the cottonlike material failed to control bleeding satisfactorily (Table I).

In general surgical and neurosurgical cases the absorbable oxidized cellulose was not removed before closure of the incision regardless of whether drainage was established. Delayed healing of the incision such as could be attributed to the presence of a foreign body did not occur. There was no unexplained postoperative febrile reaction.

In the otolaryngologic cases the absorbable oxidized cellulose usually was removed at the time of the first dressing, that is, on the 5th day after the operation. The material was so gelatinous that it was removed with a suction cannula without difficulty. The cavities were clean. Bleeding, which is so likely to follow removal of the usual gauze packing, did not occur. Drs. H. L. Williams and O. E. Hallberg of the department of otolaryngology and rhinology, found that absorbable oxidized cellulose was more satisfactory than ordinary gauze for packing wounds. In the fenestration operation the use of the material to hold the flap in place and to prevent seepage of blood postoperatively seems superior to any method previously used. Drs. Williams and Hallberg commented on the absence of the usual granulation tissue when absorbable oxidized cellulose was used and on the elimination of the arduous and painful task of removing ordinary gauze. The presence of infection was no contraindication to the use of this material.

PATHOLOGIC STUDIES

Two and a half days after a wound of the brain had been filled with oxidized cellulose, small pieces of fiber resembling cotton fiber were found in a specimen obtained from the wound. The specimen was placed in a 10 per cent solution of formalin and when it was removed for sectioning, a few fibers remained. It was, therefore, decided to test various fixatives to determine their suitability in connection with the use of oxidized cellulose.

Small portions of both the cottonlike and gauzelike material were placed in various solvents. In plain water, oxidized cellulose was about half destroyed by the 3d day. The same occurred in saline solution. In a 5 per cent solution of sodium bicarbonate, oxidized cellulose disappeared in about 20 minutes. In a 10 per cent solution of formalin, there was after the first day disintegration, grade 2, on

the basis of 1 to 4, in which 1 designates the most and 4 the least disintegration. At the end of the 3d day, it was difficult to identify any residue of the cellulose. In a 70 per cent solution of alcohol, the cellulose became somewhat fluffy and soft, while in 95 per cent absolute alcohol, it underwent no change either macroscopically or microscopically. In methyl alcohol, there was some slight softening of the cellulose after 3 days. Zenker's solution and Bouin's fluid caused considerable discoloration and marked brittling of the cellulose so that it fragmented when picked up. Microscopic sections, in which there was approximately grade 2 to 3 disintegration of the cellulose after 3 days, were examined at intervals until the 7th day. The persistent portion appeared to be small eosinophilic masses which were irregularly placed throughout the section. All elements of the tissue appeared to disintegrate at the same rate of speed.

Some collected pooled serum and pieces of gauzelike material were placed in a series of tubes and examined at daily intervals. On the 1st day, there was slight disintegration and fuzziness of the cellulose, and on 4th day, disintegration, grade 3. By 7th day, few fibers were present. The serum was not kept at 37 degrees C., that is, at body temperature. Whether this would cause an increase in the dissolution of the gauze has not been determined.

When oxidized cellulose was placed in whole blood, there was grade 2 dissolution after the 1st day; by the 3d day, only an occasional fibril and by 4th and 7th days, none. This indicated that dissolution began on about the 2d day and reached a maximum on 7th day. Whether body temperature or incubation would hasten this process, has not been determined.

The best fixative appears to be either 95 per cent or absolute alcohol. This fixes the tissue with no further dissolution of the cellulose when the specimen is put into other fixatives.

Cellulose that had been left in wounds for 2½ and 4½ days, respectively, also was examined. After 2½ days, some small eosinophilic masses, resembling the material previously mentioned, remained. There was only slight polymorphonuclear leucocytic reaction and the remaining particles of cellulose were mingled with fibrin, erythrocytes, and necrotic brain substance. At 4½ days, this process had progressed so that no fibers were seen.

CONCLUSIONS

Specially prepared absorbable oxidized cellulose, either gauzelike or cottonlike in type, with a solution of thrombin, was tried by various surgeons of the Mayo Clinic as an aid to hemostasis in 60 cases. Results were encouraging; hemostasis was excellent and immediate in 37 cases and satisfactory in 20 cases.

The hemostatic effect of oxidized cellulose seems to depend on its sticky character when saturated with blood. It produces minimum tissue reaction and is relatively nonirritating and readily absorbable. It can be removed from a wound without the secondary bleeding that so frequently occurs after removal of ordinary gauze. Since cellulose is a foreign body, however, use of a large amount of it in a deep, nondrained wound may be unwise.

In pathologic studies the pathologist found no fibers remaining in the tissue 4½ days after the material had been introduced into the wound. The reaction in the tissue was limited to presence of a few polymorphonuclear cells.

The results of this study would seem to justify further clinical trial of absorbable oxidized cellulose, both with and without thrombin. In a few recent cases excellent hemostasis has been obtained with cellulose without thrombin. The field of applicability seems wide and uses other than as a hemostatic agent are possible; however, it should not be substituted for careful surgical technique.

REFERENCES

1. Cronkite, E. P., Deaver, J. M., and Lozner, E. L. War Med., Par., 1944, 5: 80–82.
2. Frantz, Virginia K. Ann. Surg., 1943, 118: 116–126.
3. Frantz, Virginia K., Clarke, H. T., and Lattes, Raffaele. Ann. Surg., 1944, 120: 181–198.
4. Galbraith, J. G. Quoted by Frantz, Virginia K.
5. Ingraham, F. D., and Bailey, O. T. J. Neurosurg., 1944, 1: 23–39.
6. Ingraham, F. D., Bailey, O. T., and Nulsen, F. E. J. Neurosurg., 1944, 1: 171–181.
7. Putnam, T. J. Ann. Surg., 1943, 118: 127–129.
8. Seegers, W. H., and Doub, Leonard. Proc. Soc. Exp. Biol., N.Y., 1944, 56: 72–73.
9. Unruh, C. C., and Kenyon, W. O. J. Am. Chem. Soc., 1942, 64: 127–131.
10. Williams, H. L., and Hallberg, O. E. Personal communication to authors.
11. Yackel E. C., and Kenyon, W. O. J. Am. Chem. Soc., 1942, 64: 121–127.

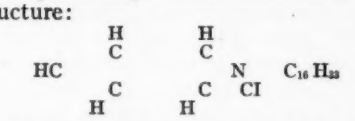
A CLINICAL APPRAISAL OF CETYLPYRIDINIUM CHLORIDE AS A SKIN ANTISEPTIC

JAMES A. HELMSWORTH, M.D., and PAUL I. HOXWORTH, M.D., Cincinnati, Ohio

In vitro experiments (2) indicate that solutions of cetylpyridinium chloride have marked germicidal activity. The purpose of this investigation is to study the efficacy of these solutions when used to prepare the skin preoperatively in the surgical clinic. The limitations of skin degerming processes are well known. In presenting this study it is realized that no method or agent or combination of the two in clinical use at the present will consistently sterilize the skin. Clinical methods are quantitative degerming procedures. The organisms have their numbers reduced but cannot be eliminated in 100 per cent of trials.

Because cetylpyridinium chloride is not well known to the clinician its characteristics and properties will be briefly reviewed. In 1916 Jacobs and coworkers (6, 7, 8) pointed out that this group of compounds has strong germicidal properties. More recently Miller and Baker (10) and Harrison and Miller (1) compared the *in vitro* properties of soap and certain cationic detergents. Soaps fall into the group of anionic detergents since in them the alkyl radical carries a negative charge. Cationic detergents are so named because their alkyl radical carries a positive charge. The method of these workers was to study the metabolism of freshly prepared suspensions of micro-organisms in the Warburg manometric apparatus. In their study of 6 gram-negative and 6 gram-positive organisms they found that the cationic detergent is a more general inhibitor of bacterial metabolism than the anionic. They concluded that while gram-positive and gram-negative micro-organisms were equally sensitive to the action of cationic detergents, the anionic detergents studied selectively inhibited the metabolism of the gram-positive organisms. They state (1): "studies of homologous series of straight chain alkyl sulfates and sulfoacetates (C_8 to C_{18}) demonstrate that maximum inhibition is exerted by the 12, 14, and 16 carbon compound (lauryl, myristyl, and cetyl)."

Cetylpyridinium chloride, a cationic detergent, is a quaternary ammonium salt having this structure:



It is a white, crystalline solid which dissolves readily in water, forming an odorless solution slightly alkaline in reaction. It is sometimes called an invert soap, differing from other soaps in containing no metallic base and in being chemically reversed in respect to the electrical charges of the group in the molecule. This product has both hydrophilic and lipophilic properties. The hydrophilic properties originate from the ionic properties of the salt and the lipophilic properties originate from the long chain structure of the cetylpyridinium cation which is attracted to lipoids. When cetylpyridinium chloride is placed in contact with water and lipoids a definite orientation of arrangement establishes contact with both types of matter and is responsible for a high tissue penetrating action. This solution, with its wetting and detergent properties, has increased power to penetrate pores and minute crevices. The importance of such properties in a skin sterilizing agent need not be emphasized. Dilute solutions of this salt do not precipitate blood serum or egg albumen. By more concentrated solutions the proteins are precipitated but redissolve on addition of more cetylpyridinium chloride. *In vitro* experiments (2) indicate that the presence of serum does not abolish the compound's germicidal activity. The germicidal potency of all quaternary ammonium salts is reduced by soaps. However, no other significant incompatibility has been discovered.

From the Department of Surgery, College of Medicine, University of Cincinnati, and the Cincinnati General Hospital.

In *invitro* experiments comparing germicidal activity against Staphylococcus aureus, cetylpyridinium chloride was shown by Blubaugh, Botts and Gerwe (3) to be superior to all other compounds tested. Blubaugh and coworkers (4) demonstrated too that this germicidal effect is not a selective one but is exerted against all the common pathogens. Further study by Green and Birkeland (5) indicates that cetylpyridinium chloride is an effective germicide for bacterial spores.

Warren, Becker, Marsh, and Shelton (11) have reported the pharmacological and toxicological properties of this compound. The alleged "curare-like" action of toxic doses has been confirmed. In experiments for the study of acute and chronic toxicity it was found that doses many times larger than a patient would ever receive were required to produce untoward effects in the experimental animal. Also no significant irritative effect was found when it was applied to the skin and mucosal surfaces of patients.

METHOD

With the experimental background for the use of cetylpyridinium chloride as a germicide established, an attempt at clinical evaluation of this agent was undertaken. It must be strongly emphasized that this study includes numerous possibilities for error in its experimental method. The sterile media and the cultures were transported several miles from laboratory to operating room by untrained personnel. The preparation of each operative site was supervised by one of a group of ten house officers. It is inevitable that there should have been minor variations introduced by individual surgeons. The opening and closing of the culture bottles was done by nurses and operating room aids whose training in bacteriologic technique was more or less deficient. These are but a few significant variants which were not controlled.

In this investigation the pathogenicity of the contaminants was not determined. The microscopic examination showed the morphology to be, for the most part, large gram-positive cocci and rods similar to the nonpathogenic air contaminants frequently encountered in routine culture work.

TECHNIQUE

For *experiment 1* the operative site was shaved in the usual way, soap and water lather being used. This preparation was done on the ward the night before operation or in the operating room as the initial step in the preparation. A cotton swab culture (the swab dipped in sterile normal saline solution or distilled water) was taken from the operative field after the simple cleansing of the skin with soap and water, alcohol, and ether. A second swab culture was taken from the area after application of the tincture of cetylpyridinium chloride. Then, by means of the same technique that is used for taking pinch grafts, a small fragment of skin for culture was taken from the center of the painted area. All specimens for culture were placed in beef infusion broth at once and transferred to the incubator. The concentration of skin antiseptic and the volume of broth in the culture container were changed during this experiment.

For *experiment 2* the operative site was shaved as here outlined. A cotton swab culture was taken from the operative field after it had been scrubbed in a rotary pattern, cotton gauze soaked with 1:100 aqueous solution of cetylpyridinium chloride being used. This was done by one of the operator's assistants before he had prepared his own hands and arms by scrubbing. The gauze used was not sterilized. The preceding two details apply also to experiments 3 and 4. Ten minutes were to have been spent in the scrubbing process, though it is probable that in some cases the period was shortened. The gauze sponge was changed for a freshly soaked one four to six times during the scrub of each field. A second swab culture was taken from the same area after the application of the tincture of cetylpyridinium chloride. Then, as in experiment 1, a small piece of skin for culture was taken from the center of the prepared area.

For *experiment 3* the patient was shaved on the ward or in the operating room, but the usual soap and water lather was replaced by the 1:100 aqueous solution of cetylpyridinium chloride. It was thought that any soap left on the skin after shaving might reduce the effectiveness of the cetylpyridinium chloride used subsequently. Because of the well known

"incompatibility" which had been demonstrated *in vitro* it was proposed to eliminate any such reaction in the clinical application of the germicide. No attempt at special cleansing was made at the time of the shaving. As in experiment 2, the cotton swab culture was taken from the operative field after it had been scrubbed 10 minutes with gauze soaked in 1:100 aqueous cetylpyridinium chloride. The skin fragment was taken from the prepared area as in the other experiments. No tincture was added to the field prepared by this single washing process.

In *experiment 4* the preparation of the operative site was further simplified. As in experiment number 3, shaving was done with the 1:100 aqueous cetylpyridinium chloride instead of soap and water lather. However, the cotton swab culture was taken from the operative field after that area had been scrubbed only 5 minutes with gauze soaked in 1:100 aqueous cetylpyridinium chloride. The skin fragment was then taken for culture as in all other experiments. The incision was made without further treatment of the field.

All cultures were incubated 7 days at 37 degrees C. Daily observations were made for the growth of contaminants. In experiments 3 and 4 mixed suspensions of Staphylococcus aureus and Escherichia coli (one 24 hour culture of each) diluted to perceptible cloudiness (approximately one-half billion organisms per c.c.) in 0.1 cubic centimeter amounts were added to each bottle which showed no growth. All were incubated at 37 degrees C. All inoculated samples supported growth of the inoculum in 24 hours.

DATA AND OBSERVATIONS

1. Bacteriologic studies. Experiment 1 may be divided into two parts. In part A the skin was painted with 1:1000 tincture of cetylpyridinium chloride. It was decided to use a more concentrated tincture after 122 cases had been collected. Accordingly, in part B, the 1:500 tincture was used, and the results recorded in the first 122 cases. This group is used because it is comparable with the series in which the 1:1000 tincture was used.

Part C covers 395 cases inclusive of those listed in part B, and consists of the total cases in the series in which the 1:500 tincture was used. It should be explained that there were 411 cases in the original group. In 16 of these it was found that there was a positive culture after the application of tincture, though the swab culture taken after simple washing had failed to show any contaminant. Several factors may figure in the explanation of this. The swab may have failed to pick up organisms that were still present and viable after the washing and were picked up after the application of the tincture. The swab may have carried enough soap and water to inhibit the growth of bacteria carried to the 10 cubic centimeters of broth. The same effect may have been lost by the dilution factor when organisms were carried from the painted surface to the 150 cubic centimeters of broth. Or these may be cases in which there was contamination from the outside after the application of the tincture. It is apparent that these cases of negative culture after the wash but positive culture after the application of tincture should be eliminated from any series which attempts to evaluate the clinical germicidal value of the tincture.

A comparison of results of part A with part B suggests several points. In this particular study, washing the skin with soap and water, alcohol, and ether was not very effective as determined by the swab culture method. There were positive cultures in 78.7 per cent of the cases of the first series and 86.1 per cent of cases of the second. Lee and Hoxworth found contamination in only 22.6 per cent of their series of 216 cases. It should be noted that careful standardization of the technique of the soap and water, alcohol, and ether wash was not done. This step in the procedure was regarded as a preliminary to the application of the skin antiseptic, and such important factors as length of time of scrubbing were not regulated. It is certain, however, that our procedure was comparable with that of Lee and Hoxworth. So it may be said that such a preliminary skin preparation with soap and water, alcohol, and ether may vary widely in effectiveness (22.6% to 86.1% positive cultures) measured by swab culture.

Further comparison of results in parts A and B shows that the concentrated tincture

may not have been more germicidal than the dilute as estimated by swab cultures in the 2 groups of cases (53.3% in part B and 55.7% in part A). Cultures of the skin fragments suggest that, in the deeper levels of the skin, the 1:500 tincture may have exerted a greater germicidal effect than the 1:1000 tincture (37.7% in part B and 58.2% in part A). It should be pointed out, however, that the formation of conclusions from a study of groups of this size may not be justified. This point becomes obvious on comparison of part B with part C. The methods applied to those two groups were identical. Part B was formed of the first 122 cases. Part C included part B and 273 more cases. The differences that exist between parts B and C are the variations found in comparing a group of 122 with a second group of 395 of exactly the same cases. It is plain that groups of 122 may not form bases from which to draw detailed conclusions.

Finally, consideration of the frequency of positive cultures, 27.6 per cent in the skin fragments, brings out the conclusion that this method of preliminary scrubbing with soap and water and application of tincture of cetylpyridinium chloride is not very effective against organisms in the deeper layers of the skin.

Experiment 2 is considered in two parts before considering it as a whole. In part A the swab culture obtained after the application of cetylpyridinium chloride wash was placed in a tube containing 10 cubic centimeters of broth. In part B the swab obtained after the wash was placed in a bottle containing 150 cubic centimeters of broth. This change in experiment plan was made to reduce the effect of the trace of cetylpyridinium chloride solution which must be carried by the swab from the washed surface to the culture media.

Comparison of part A with part B of experiment 2 shows that in part A, cultures taken after the initial cetylpyridinium chloride wash, there were contaminants in 4.1 per cent of cases, while in part B there were contaminants in 9.9 per cent of cases. Before concluding that this difference in number of positive cultures came as a result of dilution of the germicide carried into the media by the swab it should be noted that on comparison of positive cultures found after application of the tincture and in the skin fragments there is a difference of equal magnitude between parts A and B. Since there was no alteration in the experiment plan related to these two groups of cultures, it suggests that all the differences in percentage of positive cultures may have come from the same cause and that the introduction of a dilution factor failed to disclose any definite bacteriostatic effect by the cetylpyridinium chloride carried to the culture media.

In part C of experiment 2 several points are obvious. If the swab culture method can be relied upon to give a sample of surface flora, the simple method of scrubbing with the solution of cetylpyridinium chloride is an effective method for killing bacteria on the skin's surface. After this wash there were positive cultures in 6.3 per cent of the cases. The application of the tincture did not definitely augment the bactericidal process. There were contaminants then in 5.9 per cent of the cases.

The most striking results were found on culture of the skin fragments. Here positive cultures were found in only 3 per cent of the cases. The reason for the smaller number of positive cultures from the fragments than from the skin surface is not clear. Organic matter on the skin at the time of the washing may inhibit the activity of the agent and so allow growth of organisms in swab cultures. The swab cultures of the surface covered an area many times greater than the surface area of the skin fragment. The fragment may have carried with it to the media enough of the agent to effect some degree of bacteriostasis. Tissue fluid from the bit of skin may have acted with the cetylpyridinium chloride in a synergistic way.

In experiment 3, the skin of 257 patients was shaved, 1:100 aqueous cetylpyridinium chloride being used. Cultures were taken by swab and skin fragment after a 10 minute scrub with the same aqueous solution. The swab culture was positive in 15.6 per cent of the cases. Five and four tenths per cent of the skin fragments cultured showed contamination. In detailing the technique it was suggested that because soap is known to reduce the germicidal activity of cetylpyridinium chloride *in vitro* the bactericidal effect of this

agent might be increased by eliminating all traces of soap from the area being prepared. In experiment 2, the skin of 271 patients was shaved with soap and water and cultured by swab after a 10 minute scrub with 1:100 aqueous solution of cetylpyridinium chloride. Five and nine tenths per cent of the swab cultures showed contamination. In this third experiment where no trace of soap could have been on the skin 15.6 per cent of the swab cultures showed contamination. It would seem that any trace of soap left on the skin after the usual shave did not have a significant effect upon the germicidal activity of the aqueous solution of the cetylpyridinium chloride. Only the swab culture results are compared because the skin fragment results are not comparable. In experiment 2, 1:200 tincture of cetylpyridinium chloride was added to the skin before the fragment was cut.

In the fourth experiment, the skin of 232 patients was shaved, 1:100 aqueous cetylpyridinium chloride being used. Cultures were taken by swab and skin fragment methods after a 5 minute scrub with the same aqueous solution. The swab culture showed 13.8 per cent of the cases to be contaminated. Ten and three tenths per cent of the skin fragments cultured showed contamination. This latter finding may indicate that the germicidal effect obtained by the 10 minute scrub is greater than that obtained in 5 minutes of scrubbing (5.4 per cent positive cultures compared with 10.3 per cent). Change of the scrubbing time from 10 to 5 minutes made no significant difference in results obtained by swab culture (15.6 per cent positive cultures compared with 13.8 per cent).

As described in the technique, mixed suspensions of Staphylococcus aureus and Escherichia coli in 0.1 cubic centimeter amounts were added to each bottle which showed no growth in experiments 3 and 4. All bottles supported growth of the inoculum in 24 hours. That this finding is of some significance is suggested by the report of Lee and Hoxworth. They concluded that the apparent high degree of effectiveness of ethyl mercurithiosalicyate (merthiolate) indicated in their swab culture study was probably due to the bacteriostatic effect of that agent carried on the swab into the culture media. Because all negative cultures in experiments 3 and 4 supported growth of the inoculum it appears that such a misleading bacteriostatic effect was not present in this study.

2. Physical characteristics. All dilutions of the tincture are now tinted with a special reagent dye. In all alkaline medium, as in the presence of traces of soap, it changes from its red-orange color to a yellow-orange. This warns of the incompatibility which has already been mentioned. It coats the skin surface smoothly and its color sharply demarcates the prepared area.

The aqueous solution of cetylpyridinium chloride being colorless, odorless, and practically tasteless is easily used as a germicide. When used in the scrubbing process it forms a fine, colorless foam not unlike that of white soap and water.

3. Delayed and secondary effects. In one case in the entire group there was local vesiculation and erythema suggesting an allergic reaction. While experiment 4 was being conducted a small number of patients were found to have vesicles beneath the adhesive tape at the periphery of the operative site. The cause of this reaction may include several factors. It was found only when the adhesive was in direct contact with the skin. Change in adhesive tape has been apparent to all users in the past year. The skin had been coated with tincture of benzoin before the application of the tape. The composition of the tincture of benzoin may have been altered during the past year. The patients showing the reaction were often those who had lain 1 to 3 hours on linen soaked in 1:100 aqueous solution of cetylpyridinium chloride. The reaction may have resulted from overlong contact with the germicide.

The reactions mentioned were not of a nature to limit in any way the use of the 1:100 aqueous solution of cetylpyridinium chloride.

4. Applicability of method. Before this study at the Cincinnati General Hospital the operative field in all cases was first cleansed in the operating room with soap and water, alcohol, and ether. The technique of experiment 2 did not include this step. It was replaced by the simpler method of scrubbing

with the germicidal solution. In experiment 3 the procedure was further simplified. The application of the tincture to the operative site was eliminated. Experiment 4 employed a method equally simple with the additional advantage of reduction in time required for preparation of the operative site. It is our opinion that methods employing the fewest agents and requiring less time will be most efficiently carried out by operating room personnel. The conservation of time will be a detail of some importance to the surgeon.

5. *Economy.* A study was made of the cost incurred by using 1:100 aqueous solution of cetylpyridinium chloride as the sole agent in preparing an operative field. A contrast study was made of the cost with soap, water, alcohol, ether, and various tinctures. The cost of the former method was much less than half that of the latter.

SUMMARY

1. The physical characteristics, the bactericidal properties *in vitro*, and the pharmacological and toxicological properties of the germicidal agent, cetylpyridinium chloride, have been reviewed.

2. A clinical study of the germicidal activity of two dilutions of a tincture of cetylpyridinium chloride has been presented.

3. A clinical study of bactericidal effect has been presented in which the operative site was scrubbed 10 minutes with an aqueous solution of cetylpyridinium chloride and then painted with a tinctue of cetylpyridinium chloride.

4. A clinical study of bactericidal effect has been presented in which the operative site was scrubbed with 1:100 aqueous solution of cetylpyridinium chloride in one experiment 10 minutes and in another 5. No further treatment was given the site in this group of cases.

CONCLUSIONS

1. The preliminary preoperative skin preparation with soap and water, alcohol, and ether may not be an efficient germicidal process if all details of the procedure are not carefully controlled.

2. Tincture of cetylpyridinium chloride applied to operative fields washed with soap and water, alcohol, and ether has a definite germicidal effect.

3. Scrubbing operative fields with a 1:100 aqueous solution of cetylpyridinium chloride produced a striking germicidal effect.

4. Aqueous solution of cetylpyridinium chloride is well tolerated by the skin of patients. Its physical characteristics make it acceptable to operators and its use is economical.

REFERENCES

1. Baker, Z., Harrison, R. W., and Miller, B. F. J. Exp. M., 1941, 73:249–271.
2. Blubaugh, L. V., Botts, C. W., and Gerwe, E. A study of the germicidal properties of cetyl pyridinium chloride. Proc., Forty-first General Meeting, Soc. Am. Bacteriol. 1940, 51. (Abstract, J. Bact., vol. 39.)
3. Idem. A preliminary investigation of the germicidal activity of cetylpyridinium chloride. Columbus Meeting, Ohio Branch, Soc. Am. Bacteriol. 1939 (Dec. 2).
4. Idem. A study of the germicidal properties of cetylpyridinium chloride. New Haven Meeting, Soc. Am. Bacteriol. 1939. (Dec. 28).
5. Green, T. W., and Birkeland, J. M. J. Bact., Balt. (Abstr.), 1941, 41: 34.
6. Jacobs, Walter A. J. Exp. Med., 1916, 24: 563–568.
7. Jacobs, Walter A., Heidelberger, M., and Amoss, H. L. J. Exp. M., 1916, 23: 569–576.
8. Jacobs, Walter A., Heidelberger, M., and Bull, C. G. J. Exp. M., 1916, 23:577–599.
9. Lee, M., and Hoxworth, P. I. Surgery, 1939, 6: 762–769.
10. Miller, B. F., and Baker, Z. Science, 1940, 91: 624–625.
11. Warren, M. R., Becker, T. J., Marsh, D. G., and Shelton, R. S. J. Pharm. Exp. Ther., 1942, 74: 401–408.

TREATMENT OF POSTOPERATIVE INFECTIONS FOLLOWING INTERNAL FIXATION FOR FRACTURE OF THE NECK OF THE FEMUR

KELLOGG SPEED, M.D., F.A.C.S., Chicago, Illinois

THE frequency and gravity of postoperative infections following internal fixation for fracture of the neck of the femur are not appreciated because many instances are concealed and few are reported. In a recent well ordered article Siris and associate, reporting 157 instances of fracture of the neck of the femur, cited 53 operations for internal fixation, 47 with the Smith-Petersen nail, 5 with this nail plus the Hawley bar, 1 by Moore's pins, 1 by external fixation with the Roger Anderson apparatus (which became infected) and 3 by Russell traction. The total mortality was 5, equalling 9.6 per cent. Six instances of external pin insertions, one intracapsular and 5 extracapsular fractures of the femur (intertrochanteric?) after operation developed infection at the site of pin insertions, 5 died, and the authors say, "If other surgeons have experienced the same disastrous consequences we have not found any mention of it in the literature." Neither have I. Yet I have been seeing and struggling with these calamities for several years.

I wish to confine my report to the title given, namely postoperative infection following clean, elective internal fixation for fracture of the neck of the femur, assuming that the operation has been faithfully and properly performed by a competent surgeon and not by a casual operator. Also that the operation was performed in a hospital operating room under the usual aseptic conditions for such procedure, that proper (and hopefully a three series program) roentgenologic control has been used in the fixation, and that the postoperative care of the wound and patient has been standard and adequate.

Some of these operative wounds will become infected even as a certain percentage of all clean, elective operations still plague us with infection notwithstanding our best efforts at prevention and the rapidity and skill with which operation is performed. The early and local infection and osteomyelitis in the neck of the femur set up after internal fixation may not be caused by any definite local lowered resistance of the bone. It may be attributed to local thrombosis following the fracture of the bone, to which is added the additional trauma of the inserted foreign body. The local trauma set up by the fixation agent alone in an old fracture, with long since subsided and absorbed hematoma of the acute bone severance, may be enough to cause local thrombosis and possibly necrosis. This may be aggravated by prolonged or unskillful insertion of guide wires and fixation agents, or their several times repeated withdrawal and reinsertion to correct positions. Naturally any blood stream infection may lodge in this area for settlement and growth, or the slightest amount of inborne infection on fixation nail, skin, or tissues of patient or usual sources from gloves and respiratory systems of the operators, hematoma formation, or poor skin closure may start the affair. It does happen.

These patients come to the consulting surgeon or into the services of charity hospitals, generally late, from 3 to 12 months after occurrence of infection. The onset is usually insidious and not alarming. Failure of recognition of the magnitude of the situation is not uncommon. Attempts at renailing, if nails have slipped or distraction of fracture surfaces has occurred, may unhappily be made. But usually the fixation agent is finally withdrawn by the primary operator or a colleague, and little else is done. The patient drifts into a condition of chronic osteomyelitis with bed confinement, is almost always without fixation in plaster splints, and, the surgeon hoping for a miracle, may give doses of sulfa drugs or

From the Presbyterian Hospital and the Department of Surgery of Rush Medical College of the University of Illinois.

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penicillin or both. Loss of weight and strength ensue; discharging sinuses appear at the hip, death of the head of the femur may be realized and pathological dislocation at the hip finally discovered. The patient may proceed to death from this exhaustive sepsis because in some instances the sepsis involves the acetabulum, the ilium, and the trochanteric portion, if not the shaft, of the femur. Decubitus ulcers are almost always found. The head of the femur, although dead or lying in the infected area, may unite with the neck of the femur if the internal fixation job has been well carried out.

As a result of the sepsis and frequent lack of external splinting, dislocation at the septic hip may occur before or after the internal fixation agent is removed. The head of the femur may retain its fixed relationship with the neck even if united only in part. Such a head on removal is found to be eroded and necrosed, not so much on cartilaginous and joint surface as on posterior aspect, possibly on account of a gravity pool of pus forming posteriorly as patient lies in bed or splint.

If the infection in the track of the fixation agent and the hip joint is recognized early, the use of sulfa drugs or penicillin with immobilization may control it before local bone death and free pus formation occur. I have never yet seen such an instance. If free pus and abscess form, chemotherapy will be effective only when accompanied by free and yet nondestructive drainage of the hip joint area, along with the removal of the fixation agent and dead bone, followed by the application of a wick drain with vaseline gauze and long continued immobilization. Patients who are desperately depressed from the sepsis and malnutrition require long preparation with blood transfusions and hyperalimentation before operation for extensive drainage, manipulative proceedings, or sequestrectomy is possible. Skeletal traction on the leg is of great assistance in these operations to aid in the manipulative procedure and for postoperative sure fixation in the chosen position of traction and abduction of the leg. Operations for primary bone shelf support above the acetabulum, nail, screw, or bone transplant fixation to the pelvis, osteotomy, or arthroplasty do not seem wise in the presence of the extensive gross infection about the hips.

In young patients, when infection has subsided for many months, secondary operations may be indicated for great looseness of the hip, pain on weight bearing, or embarrassing shortening of the leg after use. Such a late operation may be desirable to give better functional and cosmetic results. A final movable hip may be better for some patients than a solid bony ankylosis; in most instances healing with a flexed or abnormally angled hip can be bettered by osteotomy and restoration of better weight bearing axis. The treatment may be summarized as follows:

1. Recognize infection, identify organism.
2. Prepare patient for operation.
3. Insert Steinmann pin through tibia or heel, withdraw fixation agent in hip, remove head of femur (do not cut off greater trochanter), replace neck in acetabulum, apply narrow vaseline gauze drain, and administer sulfa drug locally.
4. Close most of wound, apply body plaster with leg in slight abduction.
5. Start penicillin 100,000 units first 24 hours intravenously, 10,000 units every 4 hours thereafter.
6. Leave immobilized until sinus is healed and bony union attained, if possible.
7. Operate later for reconstruction of hip if needed.

CASE 1. G. M., male, aged 54 years, on April 6, 1938, had a fracture of the neck of the left femur. Three steel pins were inserted after good reduction shown in the posteroanterior roentgenogram, April 7, 1938; no lateral roentgenogram was taken. Wound infection followed. By August 5, 1938, the pins had been removed, the head of the femur was now rotated and in valgus position because there had been traction on the leg and no union at the neck. By August 31, 1938, this condition was enhanced and the rotated head of the femur had come completely out of the acetabulum. In September, 1938, the head showed increased density, irregularity, and spotty absorption—dead. The upper margin of the acetabulum began to melt away and there appeared a doubtful extension of the osteitis into the trochanteric portion of the femur and down the shaft where there were areas of spotty absorption and new bone formation beneath the periosteum. Pus (staphylococcus) drained freely from hip. Thigh was soggy, fluctuant. Temperature reached 100 degrees daily, and there was great loss of weight and strength.

The diagnosis, when first seen by me on September 30, 1938, was ununited fracture of the neck of the femur with dead head, infected; gross infection of the left hip joint with dissolution of the acetabular margins and pathologic dislocation of the hip; osteomyelitis of the femur and ilium. He was next seen on November 8, 1938. A few attempts to get him to sit up in bed or on a chair had resulted in immediate rise of temperature. The left thigh was now enormously swollen and tender, numbness developed in the left foot, the dorsalis pedis artery was palpable, free pus discharge issued from the hip. His general appearance had deteriorated, appetite became poor; the tongue was red, glazed and dry, and he had lost weight. On November 14, 1938, he was transferred to my services at the Presbyterian Hospital. After the use of hot applications and bed rest, the left leg being supported in a Thomas splint with fixed traction from skin to splint, he was rendered afebrile, and by the last of November, 1938, he was able to be out of bed. A walking caliper was fitted to him, and the necessity of hip joint disarticulation began to fade. He was given superalimentation and encouraged to be up all he could. About February 17, 1939, temperature again rose, and considerable swelling at ankle and edema in left thigh developed.

On February 24, 1939, an operation was performed to insert skeletal traction in the left heel. An x-ray examination later showed that the femur was being pulled down and the head lay just above the upper edge of the acetabulum. Later, a forceps passed into the hip sinus struck rough, bare bone of the trochanteric region and then passed easily on up toward head of femur, but one could not tell exact source of purulent discharge. Fever still present.

On March 8, 1939, an operation on the hip was performed. After fixation on the fracture table, taking advantage of the Steinmann pin through the calcaneus for this purpose, we excised the sinus opening in the left hip by an elliptical incision 8 inches long. Pus ran out freely. The greater trochanter of the femur was cut off obliquely with a wide chisel and with muscles attached retracted back out of the way. The left leg was rotated outward and the head of the femur visualized; pus pockets were found about it. The head seemed attached in fair position by bony union to the trochanteric portion of the bone. Believing that there was deeper infection involving the ilium and acetabulum, the head of the femur was then cut off just below the level of the original fracture. When the head was thus removed, it was found that its posterior half was necrotic, greatly eroded, and covered with pyogenic granulations. The acetabular cavity could then be palpated and seen. One loose eroded piece of bone 2 centimeters long was found on the anteroinferior border lying free in pus and granulations. This probably represented a fracture of the acetabulum not clearly seen in any roentgenogram. All this cavity and granulated area was then gently curetted. By tightening the traction on the long axis of the leg, along with some inversion and abduction, the cut-off neck of the femur was inserted into the bony pocket of the ilium. The tissues were partly sutured around the upper portion of the femur. One vaseline gauze pack was laid down the axis of the neck of the femur and the main portion of the wound was approximated by through-and-through silkworm gut button sutures, the drain being left protruding. A plaster-of-paris encasement was applied, extending from the base of the left toes including the whole left leg and pelvis to costal margin and extending down the right leg to the knee.

By March 28, 1939, the final end of the vaseline gauze was withdrawn. Still some purulent drainage was noted. Temperature was normal. April 28, 1939, the nail through the left heel was withdrawn but the plaster was not disturbed. There was less drainage from the hip wound. On May 1, 1939, raw bone could no longer be felt at depth of hip sinus when sterile forcep was inserted. On May 21, 1939, he was removed from body plaster and the roentgenogram showed that cut-off neck of femur was still apposed to old curetted acetabulum, but amount of attempted bony union there could not be certified.

He gradually went on to ambulation, via a wheel chair; all discharge from the hip ceased. He was continued on sulfanilamide until August 15, 1939. About this time there was shortening of the leg, slight inversion, good pulsation in the dorsalis pedis, 30 degrees' motion in the knee joint, and he was walking, wearing a caliper support. An x-ray film showed considerable spotty absorption in the left femur but no definite areas of osteitis. He left the hospital August 22, 1939, with 2 inches' shortening of the left leg, walking on a caliper with crutches, able to get out of wheel chair and into bed alone.

At an examination on July 20, 1940, his leg was 1.5 inches short. He walked without support, presented great muscular atrophy around the left hip, no real bony fusion, the knee joint motion 90 degrees. He expected to return to work on January 1, 1941.

Final examination on October 20, 1944. He walked with a slight limp in the left leg, wearing an elevation of 1.5 inches under the left heel only. He can flex the left thigh 30 degrees, has a few degrees of abduction, stands perfectly erect, and can cross the left leg over the right. A roentgenogram at this time shows the cut-off neck of the femur quite well inserted in the old acetabular area with a well developed bony shelf at the upper margin, assuring proper support and weight bearing with a fair joint space between the head of the femur and acetabulum. The old spotty atrophy in the femur has disappeared. The recovery and reconstruction of the hip area is most satisfactory. He was advised to wear an elevation under the whole left shoe to help balance leg shortening which now equals 2 inches.

CASE 2. A. M., male, aged 46 years, was injured in Texas on January 31, 1943, sustaining a fracture of both rami of the right ischium, inferior rami of the left ischium, ala of the right ilium near the sacroiliac joint, and of the neck of the right femur. He was put in a Jones' well leg splint. The fracture of the

neck of the femur was apparently overlooked and finally recognized on April 9, 1943, with overriding and varus deformity with rotation of the head then present. On April 27, 1943, the fracture of the neck of the femur was reduced and held by a Lorenzo screw. In a few days, as no splint was used, he was allowed to walk, and shortly after came to Chicago where he was first examined by me on May 17, 1943.

A roentgenogram on this date showed an incomplete coaptation of the neck of the femur, screw still *in situ*, but the lateral roentgenogram of the hip showed that the head was rotated and angled considerably (20 degrees) although penetrated by the screw. The pelvic fractures seemed to have progressed to a satisfactory healing. On the scar of the recent operation there was a small red area, but the patient had no fever, no discharge, no signs of gross infection. He was put to bed and hot wet dressings were applied to the hip. His white blood count was 7,400 to 8,800. After a week, all redness and evidence of inflammation being gone, operation was attempted. The fractured leg measured 1 inch shorter than the opposite leg, part of which may have been caused by the inbending of the fractured pelvis.

On May 25, 1943, a modified Smith-Petersen incision was made, the scar of the first operation being excised to expose the neck and trochanter of the femur. The screw was withdrawn and cultured. A manipulation to obtain a better reduction of the head and neck was performed and the position as seen in the roentgenogram made as he lay fixed on the fracture table appeared quite satisfactory in both anteroposterior and lateral roentgenograms. After a position of satisfactory reduction, as shown by x-ray, the patient was fastened onto the Hawley table with legs in moderate abduction. A new hole was then driven into the head of the femur via the old channel of the screw in the trochanteric area, a bone transplant of suitable size and length obtained from the tibia was inserted after the position of the head and neck of the femur had first been fixed by a Moore nail inserted above the path of the reamer. The wound was closed and a plaster-of-paris encasement was applied. During this operation the patient was given 500 cubic centimeters of whole blood, and a similar amount was given starting immediately after return to bed. On May 27, 1943, patient's temperature rose to 101 degrees, and although the wound was not inspected he was put on conventional doses of sulfathiazole. Chest was normal.

On June 4, 1943, the plaster dressing was cut and the skin stitches were removed. There was some bulging of the wound, the edges of which separated and bloody pus was evacuated. Five days later his temperature was normal and it was hoped the infection was relatively superficial and under control. It did not prove to be. The wound was later opened further, the surface well dusted with sulfathiazole, and a vaseline gauze pack was inserted. By July 7, 1943, the discharge had become odoriferous; the packing and sulfathiazole were repeated. X-ray still failed to show any definite evidence of infection in head of femur or hip joint, but fever and pain continued despite gentle handling in plaster dressing. Packing and sulfathiazole at long intervals were replaced, odor and fever and amount of discharge diminished rapidly. No penicillin obtainable.

By August 17, 1943, the cast was found to be broken across the groin, permitting some movement of the right leg. The plaster had to be removed. A new x-ray examination showed to our sorrow that the head of the femur was greatly rotated, but with bone graft and pin still *in situ*. I believe this rotation occurred when I had unhappily chosen the old screw path for insertion of reamer by means of which I hoped to make a new path into head fragment.

The plaster was changed and the position not disturbed nor was the bone transplant broken, the foot and leg remaining in well corrected position. He was removed from the second plaster on September 16, 1943, with only a small fistula in the right hip, measured by probe only 1 inch deep. He was allowed a wheel chair and later crutches for ambulation without bearing weight on that right leg. Two weeks later he developed a diffuse cellulitis about the wound in the right hip which yielded to hot dressings and continued sulfa drugs until he was restored to normal temperature and finally sent home on October 23, 1943, walking with the help of crutches.

When seen a month later he had some discharge of pus from the sinus in the right hip, pain in the joint, and inability to raise his leg from the table. On December 2, 1943, an abscess around the hip wound was drained, no loose or dead bone deep in the hip region was palpated, the sinus walls were excised or curetted, sulfathiazole was implanted, and a vaseline pack inserted. A new plaster-of-paris immobilization was applied 6 days later. By December 15, 1943, his temperature was subnormal, his pain gone. X-ray pictures taken at this time failed to prove necrosis of the head of the bone; the pin and transplant were still holding.

A few tenths of a degree of temperature and some discharge from the hip persisted. X-ray examination with the help of planigraphs on January 31, 1943, showed quite certain evidence of death of the head of the femur although still fixed in the position obtained at operation.

Consequently on February 7, 1944, the old wound was reopened on the right hip and the Moore pin and the head of the femur removed after it had been split with a chisel because it was so firmly imbedded and adherent in the acetabulum. The bone transplant in the trochanteric portion of the femur was not disturbed. The hip joint area was gently curretted and wiped out. The leg was again put in a functional position and the wound was partly closed, a vaseline gauze pack being left in its depths. Body plaster was applied. Whole blood transfusion of 500 cubic centimeters was given during operation.

By February 11, 1944, his temperature was normal. The sulfathiazole was discontinued 4 days later. The cast was cut open for dressing on February 11, 1944, and a large amount of foul smelling

discharge was disclosed. The button sutures were removed and a new vaseline gauze pack was inserted; he was still fever free. This was repeated on March 1, 1944, with saturated dressings found but no fever, and a smaller pack was inserted. At this time he was given a total of one million units of penicillin in consecutive doses of 10,000 units every 4 hours. On March 15, 1944, he was removed from the plaster when there was very slight discharge, he had no fever, temperature was normal. On April 26, 1944, he went home; the sinus was practically closed. The sinus has remained closed, and he walks on crutches.

At a later examination on August 28, 1944, he could walk on crutches several blocks; he wore a support under the right foot to compensate for the shortening of that leg. The sinus was completely closed and healed. An x-ray examination showed no dead bone or sequestra and a doubtful bridge of bone union between the trochanteric fragment of the femur and old acetabulum. There was no change in the axis of femur. The foot was in excellent weight bearing position with no additional shortening.

This patient's real infection was first noted on June 4, 1943. Ten months later on April 1, 1944, penicillin was started, 100,000 units being given by continuous intravenous drip the first 24 hours, followed by 30,000 to 80,000 units intramuscularly daily thereafter until he had been given one million units.

During the course of his earlier treatment he seemed to develop an outward reaction to sulfathiazole which was given in maximal therapeutic dosage from February 5 to February 7, 1944, February 10 to February 14, 1944, and March 14 to March 30, 1944 which apparently caused a secondary rise in temperature, some cyanosis, and interference with his appetite. We concluded that the final closure of this difficult sinus was probably due to 3 factors: the drainage with removal of dead bone, the use of penicillin, and the immobilization, probably the least important of the three.

CASE 3. H.D., female, aged 54 years, fell in a distant eastern city and broke the neck of her right femur on November 29, 1943. She was taken to a hospital and a Smith-Petersen nail was inserted December 1, 1943. The films made on the operating table showed an apparent good reduction. There was an almost immediate postoperative temperature of 104 degrees and 7 days after the hip operation a probe inserted into the wound led to the evacuation of 2 ounces of "old blood" with a suspicious odor, as described by her surgeon. This on culture was "green" Staphylococcus aureus. Two days after operation she was suffering from injection of the throat and soft palate and a yellowish membranous deposit thereon. A portable roentgenogram this same day showed early patchy bronchopneumonia in both lungs. Sulfadiazine was administered. A roentgenogram on December 29, 1943, showed that the Smith-Petersen nail did not project into the head of the femur but lay on the upper anterior surface of the head fragment with angulation (coxa vara) of the head and neck of the femur and no apposition between the fracture surfaces. After consultation, it was decided to remove the pin and apply a plaster-of-paris spica to the hip. This was done on January 10, 1944, enclosing the entire right leg and the left leg to the knee. In March, 1944, the patient was given 2 courses each of 1,000,000 units of penicillin. Her fever subsided late in January except for one recrudescence up to 102 degrees on February 2, 1944. The plaster-of-paris dressing was removed April 28, 1944, and the patient was allowed to move the limb, to sit up in bed, and was found to have a right foot drop, supposedly caused by pressure of the original plaster dressing. The sinus in the right hip still continued discharging serosanguineous material.

She entered the Presbyterian Hospital, Chicago, June 5, 1944 able to walk on crutches, with a discharging sinus on the right hip, a shortening of the right leg of 2.5 inches, paralysis of the right peroneal nerve, severe pain and stiffness in the left arm and hand, white blood count of 6,300 to 7,500. The last complaint she believes has followed attempts to lift herself by a sling to an overhead bar while in plaster-of-paris. A roentgenogram of this date shows a partially dissolved and dead head of the right femur, spotty atrophy in the trochanteric portion of the femur and ilium and an upward displacement of the femur accounting for the shortening mentioned. A splint was made to support the right drop foot.

Her general condition was very good and an operation was decided on for June 6, 1944. A Steinmann pin was inserted through the right calcaneus and she was fixed onto a Hawley table. The scar of the previous operation on the right hip was completely excised, the hip joint area exposed by deep dissection without cutting off the greater trochanter of the femur and the head of that bone was found quite frozen in the acetabulum (verified by portable roentgenogram). All head fragments and the infected acetabular area were curetted out, the base of the neck was pared down, and the leg was then drawn down by traction to as near the acetabular level as possible, and abducted about 15 degrees. About 6 grams of sulfathiazole was scattered over the wound surface, which was partly sutured and a loose vaseline gauze drain was left extending to its depth. A body plaster-of-paris encasement, enclosing the nail in the right heel and extending down to the left knee was applied. During the operation the patient received 500 cubic centimeters of whole blood. She received one million units of penicillin, 100,000 on the first day of operation and about 80,000 each subsequent day. By July 25, 1944, the sinus and wound had completely and lastingly healed. On

August 31, 1944, the plaster encasement was removed. A roentgenogram showed no bony union between the trochanteric portion of the femur and the ilium, but there was no pain on motion of the hip. The foot drop was improved, but there was a considerable area of anesthesia over the dorsolateral surface of the foot. She progressed slowly. By the middle of September, 1944, she was able to walk on crutches with additional sole and heel under the right shoe and a spring support for the foot. There was no pain in the hip but considerable distress in the left hip and knee from weight bearing efforts. She left the Presbyterian Hospital October 20, 1944, walking partly without crutches, able to go up and down stairs and sit and rise alone from a chair. Numbness and drop of the right foot still persist. She expects to return to work, at least part time, in December, 1944.

CASE 4. J.D. male, aged 55 years, was injured December 31, 1943, when bumped into while ice skating, with resulting fall and fracture of the neck of the left femur. He lay in bed 10 days with skin traction on the left leg and then submitted to an operation which he said took 3 hours, 45 minutes. The neck of the femur was pinned with a modified Smith-Petersen nail; no plaster dressing or external splint was applied. A few days later when he put his hand down near the wound he encountered a discharge of pus after which some tissue came out leaving an infected wound. He remained in the hospital 3 months during which period he lost 35 pounds in weight and was then sent home in an inadequate plaster dressing with an open infected wound of the left hip which had been dressed daily.

When admitted to the Presbyterian Hospital on May 23, 1944, he was in an extremely emaciated condition: hemoglobin, 8.4 grams; red blood count, 3,000,000. He lay in bed with the left thigh slightly flexed and adducted with a discharging sinus 4 inches below the greater trochanter of the femur. He also had an indolent pressure sore 2.5 inches in diameter over the sacrum, the skin edge of which was undermined and overhanging, the bone surface forming the base. A similar smaller pressure sore existed over the head of the left fibula. An x-ray film showed a spotty absorptive process involving the left ilium and upper portion of the left femur. The fracture of the neck of the femur was ununited, the internal fixation agent had been removed, the head of the femur was necrotic and apparently septic absorption of part of the head and the neck had occurred.

The first step had to be an attempt to raise his general physical condition by the use of whole blood transfusions, vitamins, and liver extract along with as much hyperalimentation as could be forced to get him in condition for surgical operation. These efforts were pursued from May 23, 1944, to July 25, 1944. He received four whole blood transfusions of 500 cubic centimeters each during this period. Food forcing often caused diarrhoea. His hemoglobin eventually reached 14 grams.

Operation was performed July 25, 1944. A Steinmann pin was inserted through the left heel for control of the leg, the hip was exposed through heavy scar tissue, and much soft infected granulation tissue rolled out of the wound. The dead and eroded head of the femur, free and easily removable, was excavated from the hip joint. It was surrounded by bleeding granulation tissue which after curettement led to an almost uncontrollable hemorrhage on the table, finally stopped by hot packs. The leg was then drawn down by traction and slightly inverted. The ilium and acetabulum seemed to be the seat of quite extensive osteitis. The wound was partly sutured, 5 grams of sulfathiazole was placed in it along with a narrow vaseline gauze drain. A body plaster-of-paris cast was applied over whole left leg and down to right knee. He was given a blood transfusion on table and immediately afterward, totalling 1000 c.c.

By August 14, 1944, he still had a little fever. The gauze pack was withdrawn, a large amount of thick pus was evacuated. A small vaseline gauze drain was reinserted. The next day there was a great amount of pus drainage, and it was feared that hip disarticulation alone might save his life. Within 3 days the drainage lessened and in 1 week his temperature became normal.

By September 11, 1944, there was practically no discharge, and the wound seemed healed. On September 28, 1944, however, much pus was again evacuated so that the cast had to be removed and local drainage established. This procedure showed a superficial abscess pointing toward the left buttock, which was drained. The exploring finger could not feel any uncovered bone or necrotic pieces. The hip joint area seemed covered by soft and formed granulations so that no ilium or old acetabulum could be felt. A roentgenogram made as he lay on the table at this time showed no necrotic bone but there was a coaptation between the trochanteric portion of the femur and the ilium, both of which appeared in better health, with loss of spotty atrophy. It could not be determined from the roentgenogram that there was bony union between these two surfaces thus immobilized in the presence of infection for over 3 months. Gentle manipulation of the leg, made necessary by the drainage operation seemed to show that there was motion present in the hip region between the leg and pelvis. On account of his extreme emaciation and his complaint of cast pressure, although he had no pressure ulcers, we did not reapply a plaster dressing. Since operation his temperature has remained normal, amount of drainage has lessened; 2 sinuses are present and packed with vaseline gauze, but we still hope for a healing closure and final return to health with stiffened hip. He has now had a total of 3,290,000 units of penicillin.

REFERENCES

1. HENDERSON, M. S. Arch. Surg., 1937, 35: 419.
2. MECH, K. F. J. Bone Surg., 1944, 26: 444.
3. MOWLEN, R. Brit. M. J., 1944, 1: 517.
4. SIRIS, J. E. and RYAN, J. D. Surg. Gyn. Obst., 1944, 78: 63.

HYDRONEPHROSIS

Classification and Plastic Repair of Ureteropelvic Obstructions

THOMAS E. GIBSON, M.A., M.D., F.A.C.S., San Francisco, California

A SURVEY of the literature on hydronephrosis reveals the fact that today, as a result of the vast experimental and clinical research, we possess a more accurate knowledge of the mechanism of hydronephrosis and a far better appreciation of the remarkable reparative power of the kidney subsequent to release of obstruction.

Hydronephrosis follows persistent obstruction at any point in the urinary tract, from the urethral meatus to the level of the renal pelvis. One of the most common sites of obstruction is the ureteropelvic junction. Because of certain controversial points, it is important to review this phase of the subject, and particularly to evaluate the numerous plastic procedures for correction of hydronephrosis based on a classification of ureteropelvic obstructions.

HISTORICAL NOTE

Trendelenburg is given credit for the first attempt at plastic repair of hydronephrosis in 1886; the outcome in his case was unsuccessful—the patient died from intestinal obstruction. In 1892 Kuester reported the first successful plastic operation on the renal pelvis. His operation consisted in reimplantation of the sectioned ureter into the pelvis at its most dependent portion. At approximately the same time, Fenger, in a clinical lecture, described a plastic procedure which he had done for the relief of hydronephrosis due to valve formation and stricture of the ureter at the ureteropelvic junction. Fenger's method consisted of a longitudinal incision at the point of obstruction with transverse closure, an adaptation of the Heineke-Mikulicz principle used in intestinal surgery. Study of the many types of plastic procedures subsequently applied to the correction of ureteropelvic obstruction shows for the most part a close parallelism to methods that have become more or less standard in gastrointestinal surgery. The stimulus of this early work led to an era in which the renal pelvis became the recipient of surgical attention that was perhaps more enthusiastic than discriminating. There were many failures, and even those cases in which the results were termed successful must be accepted with reservation, since they antedated the development of urography with its present day precision in the evaluation of surgical end-results. Even currently, no one is justified in citing an end-result as successful without urographic evidence after a sufficient postoperative period. Silent destruction of the kidney may occur postoperatively and give a false impression of cure unless checked by careful urologic investigation.

That the earlier enthusiasm for conservative plastic surgery waned is apparent from a review of the discussion of hydronephrosis at the German Urological Congress in 1921, where the fact was disclosed that up to that time nephrectomy was the generally accepted treatment of hydronephrosis. Since then there has been a gradual recrudescence of interest in conservative plastic surgery, which received a real impetus in the symposium on hydronephrosis participated in by von Lichtenberg, Walters, Quinby, and others at the annual meeting of the American Medical Association in 1929. Reference to the symposium on hydronephrosis of the American Urological Association at Minneapolis in 1937 furnishes a good cross section of the progress that has been made, and other noteworthy contributions in the past few years have served to establish plastic surgery of ureteropelvic obstructions on a firm foundation.

CLASSIFICATION OF URETEROPELVIC OBSTRUCTIONS

Analysis of ureteropelvic obstructions shows that they may be either extrinsic or intrinsic (Fig. 1). Extrinsic obstructions are kinking and distortion of the ureteropelvic outlet by

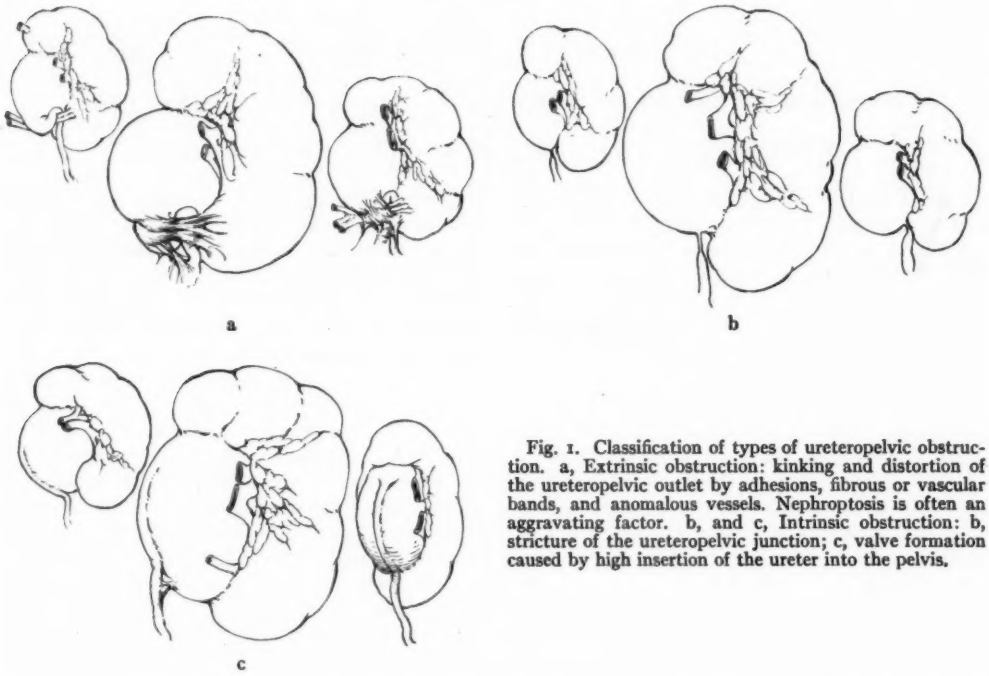

Fig. 1. Classification of types of ureteropelvic obstruction. a, Extrinsic obstruction: kinking and distortion of the ureteropelvic outlet by adhesions, fibrous or vascular bands, and anomalous vessels. Nephroptosis is often an aggravating factor. b, and c, Intrinsic obstruction: b, stricture of the ureteropelvic junction; c, valve formation caused by high insertion of the ureter into the pelvis.

adhesions, fibrous or vascular bands and anomalous vessels. Intrinsic obstructions may be subdivided into two types: (1) stricture at the ureteropelvic junction, and (2) valve formation caused by high insertion of the ureter into the pelvis. Thus, for clinical purposes obstructions at the ureteropelvic junction may be divided advantageously into three types or groups. As Deming has tersely stated, "Causes of intrinsic obstruction at the ureteropelvic junction are a thickening of the musculature, the development of hyperplastic fibrous tissue and a fibrous contracture producing a small stoma. Causes of extrinsic obstruction are strands of fibrous tissue running across the ureter at the junction and aberrant vessels." In a series of 82 cases he found intrinsic lesions in 37 and extrinsic in 50, of which 24 were due to bands of fibrous tissue and 26 to anomalous vessels. It must be borne in mind that these groups may overlap, and it is not uncommon to find in a given case a combination of intrinsic and extrinsic factors at work. This fact led Henline and Menning to emphasize the necessity, during surgical exposure, of measuring the inner caliber of the ureteropelvic junction, which cannot be judged accurately by external inspection or palpation. Thus after removal of extrinsic factors one should open the pelvis through a small incision and calibrate the outlet. This step can be done very readily by passing the tip of a Mayo hemostat or a bougie No. 12 to 14 F. down through the ureteropelvic junction, and will reveal any intrinsic obstruction.

METHODS OF PYELOPLASTY

A large number and variety of ingenious pyeloplastic procedures have evolved for the correction of obstruction at the ureteropelvic junction. The author has gathered together the principal ones which have become more or less standardized and are in current use (Figs. 2 to 8, inclusive). Analysis reduces them essentially to four basic methods:

1. Reimplantation of the sectioned ureter into the pelvis at its most dependent part

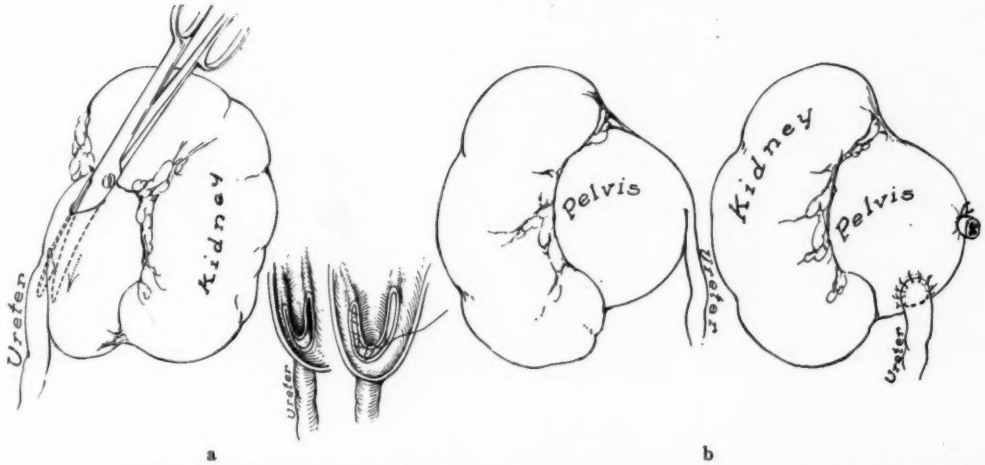

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Fig. 2. a, The first recorded pyeloureteroplasty (Trendelenburg, 1886): The ureteropelvic valve is cut downward with scissors, through high incision in pelvis. The cut edges of the ureter are sutured to the cut edges of the pelvis (inset). b, Kuester, 1892: reimplantation of ureter, ureteropyeloneostomy.

(Kuester), with or without excision of redundant pelvis.

2. Longitudinal incision with transverse closure (Fenger).

3. Y incision with V closure (Schwyzer, Foley).

4. Lateral anastomosis of pelvis and ureter.

The fourth type is essentially the original Trendelenburg operation. The Finney pelvioureteroplasty and Priestley's procedure, which includes excision of redundant pelvis, are interesting and useful variations of the same fundamental principle.

CAUSES OF FAILURE

In evaluating pyeloplastic procedures, it is necessary to pool the experience of many surgeons, because no operator has had sufficient experience with all types to determine their relative merits with any degree of authority. No single method has proved uniformly successful. Various statistical reviews indicate failure in as high as one-third of cases in some series. Ormond states that nephrectomy is too frequently performed because of unfamiliarity on the part of the profession with the conservative operations that can be effectively

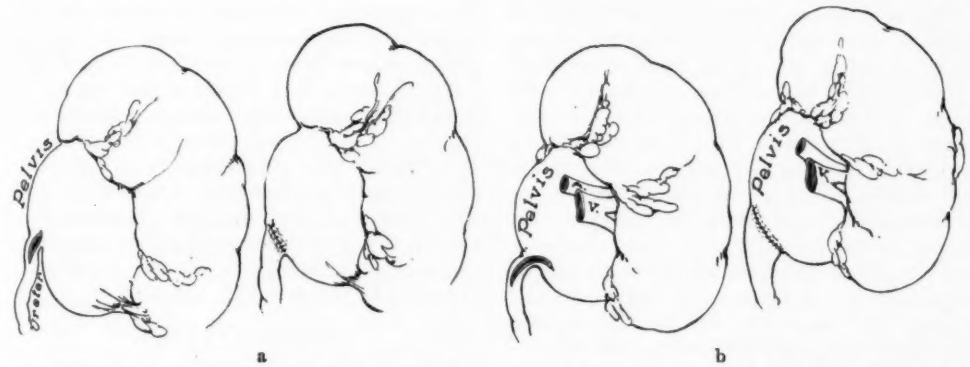

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Fig. 3. Pelvioureteroplasty. a, Pyeloplastic procedure of Fenger, 1892, adaptation of the Heineke-Mikulicz principle. b, Modification similar to Finney pyloroplasty.

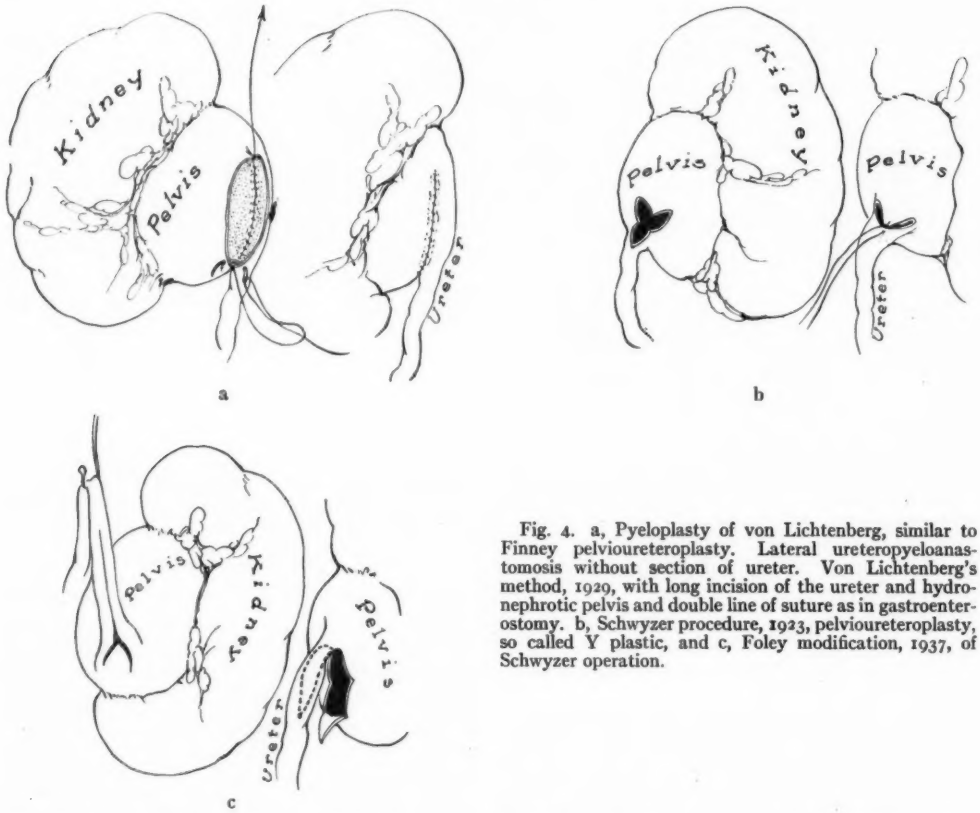


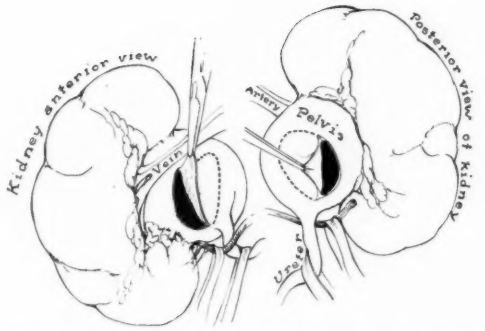
Fig. 4. a, Pyeloplasty of von Lichtenberg, similar to Finney pelvioureteroplasty. Lateral ureteropyeloanastomosis without section of ureter. Von Lichtenberg's method, 1929, with long incision of the ureter and hydronephrotic pelvis and double line of suture as in gastroenterostomy. b, Schwyzer procedure, 1923, pelvioureteroplasty, so called Y plastic, and c, Foley modification, 1937, of Schwyzer operation.

employed, lack of confidence by some surgeons in pyeloplasty as a remedy for hydronephrosis, disinclination to run the risk of failure with the embarrassment of having to do a nephrectomy at a later date, disagreement concerning the preferable type of repair and insufficient standardization of technique. Reasons for failure of plastic operations on the kidney pelvis are enumerated by Lubash as follows: (1) leakage of urine and perirenal infection at the point of anastomosis; (2) tension along the suture line with secondary infection; (3) puckering and buckling at the line of anastomosis; (4) new stricture formation, acting as a boomerang; (5) retention of urine and secondary pyelonephritis or cortical abscess formation; (6) persistent urinary fistula.

Growing experience during the past few years has shown how these pitfalls may be avoided. The fundamental principles essential to success have been elucidated so that at the present time pyeloplasty may be undertaken with far greater assurance of a successful outcome, and nephrectomy need be contemplated only in cases in which hydronephrosis is so advanced that merely a thin walled sac remains or unyielding chronic infection is present. Even in such extreme cases remarkable results may sometimes be achieved by plastic repair, particularly in solitary kidney which offers no alternative operative procedure. In such cases pyeloplasty may be a life-saving measure, as shown in Case 1 (Fig. 12) and Case 2 (Fig. 13).

SELECTION OF CASES

Poor results following pyeloplastic procedures are due not so much to the particular



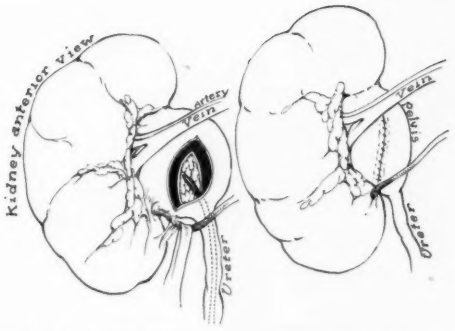


Fig. 5. Pyeloplasty of Young, 1932, with partial excision of anterior and posterior walls of pelvis to reduce size of pelvis and realign ureter so as to avoid sacrifice of aberrant blood vessels to lower pole of kidney.

method employed, but rather to improper selection of cases and failure to appreciate certain fundamental surgical principles essential to success. Whether to perform radical (nephrectomy) or conservative (pyeloplasty) surgery is not always an easy decision to make. On the basis of renal counterbalance, Hinman states that "the most skillfully performed and technically perfect plastic repair of a unilateral hydronephrosis with a normal compensatory mate is the wrong solution if it fails to put this side in the position of potential ability to carry the total load should it ever become necessary." One-quarter of the total renal mass will support life. Therefore, a hydronephrotic kidney which cannot perform 25 per cent of total function is not worth saving, although occasional exceptions may justify preserving a kidney with some 10 to 15 per cent of total function. This view would seem logically correct if one could guarantee the future integrity of the healthy compensatory mate. However, the possibility of some intercurrent pathology overtaking the sound contralateral organ and causing impairment of its function cannot be completely ignored. The increment of function of the repaired hydronephrotic kidney, however small, might contribute sufficiently to the total function to sustain life. Consequently, the fear that some catastrophe might occur which would impair the function of the good kidney prompts some urologists to perform pyeloplasty rather than nephrectomy, even in advanced cases.

With respect to determining the functional ability of the hydronephrotic kidney, Hinman states that unilateral hydronephrosis will show its full capability at the first test (if the kidney is active, uninfected, and draining freely). He further asserts that the first test will be as good as any subsequent ones, even

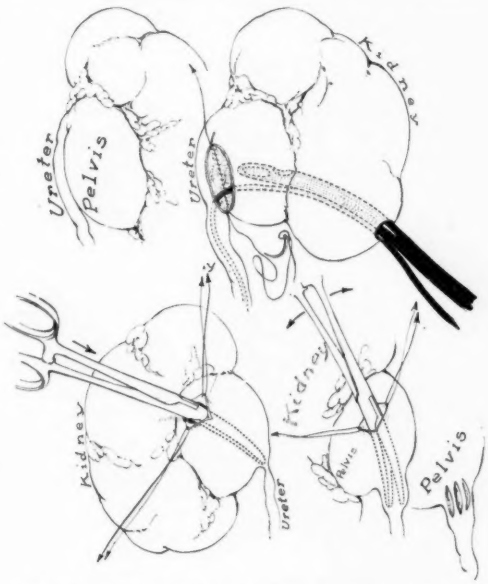
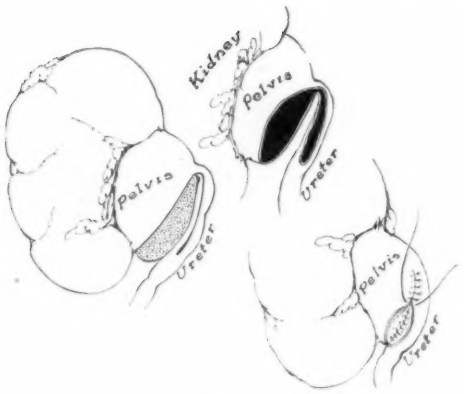
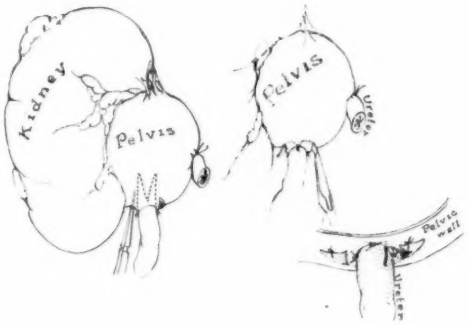


Fig. 6. a, above, Pyeloplasty imitating gastroenterostomy, anastomosis of side of ureter to pelvis. b, Davis, 1935, application of Rammstedt operation to stricture at ureteropelvic junction. Five or 6 vertical incisions are made down to the mucosa while the constricted area is dilated with a Mayo hemostat.



a

Fig. 7. a, Pyeloplasty of Priestley (1939), with excision of pelican-like pouching of the pelvis. This procedure is an improvement over the original Trendelenburg pyeloplasty.

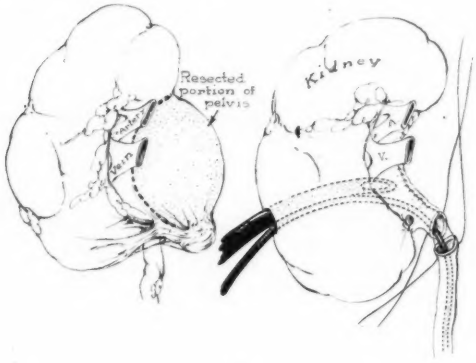


b

b, Pyeloplasty of Lubash (1937), ureteropyeloneostomy. This procedure is an elaboration of the original Kuester operation.

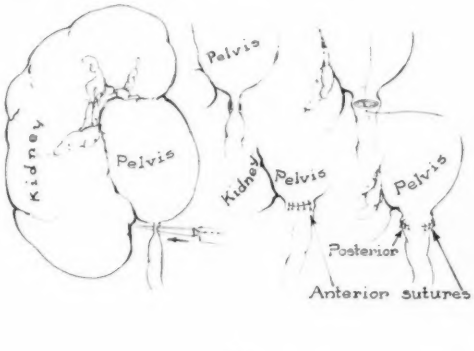
though the catheter may be retained for weeks. This is important because an uninfected hydronephrosis should not be exposed to the very considerable risk of infection which a retention catheter carries. It is, therefore, preferable to repeat ureteral catheterization and to study relative function. There are many urologists of great, if not equal, experience who take exception to these views, including the statement that "the function years after repair will be the same as at the time of repair, no more no less, with the opposite normal kidney."

From a more limited personal experience in determining the proper course of action, the tendency has been to depend less on relative function studies, which are subject to many variables, and more on the following three factors: absence or presence of infection and its severity, the pyelogram, and the appearance of the kidney at operation. One is surprised at times to find at operation an amount of parenchyma considerably in excess of that indicated from studies of function. In any event, no treatment is justified which is not based on the most complete urologic investi-



a

Fig. 8. a, Pyeloplasty using Kuester principle of ureteropyeloneostomy, but with radical excision of redundant pelvis. Radical resection of pelvis and ureter with reanastomosis of ureter to lowermost part of pelvis. This



b

operation is used extensively by Priestley and others in cases of extrarenal pelvis with constriction and distortion of upper ureter. b, Pyeloplasty applying Fenger (Gibson) operation to opposite sides of ureteropelvic junction.

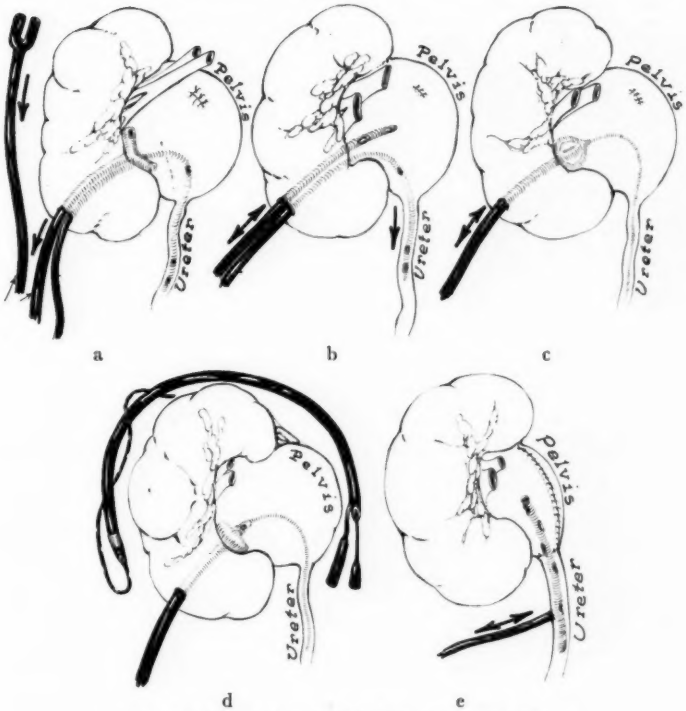


Fig. 9. Methods of ureteral splinting and nephrostomy drainage. a, urethral catheter No. 10-12F, T tube at left. b, Double eye Robinson urethral catheter No. 10-12F. c, Cumming nephrostomy tube, d, McIver nephrostomy tube. e, Ureterostomy splinting and drainage with T tube advocated by Davis-Deming.

gation, and it is usually wise to balance the findings of one complete study against those of a second confirmatory study. Sargent stressed the tendency of hydronephrosis to be bilateral and for the opposite kidney in some instances to become hydronephrotic following nephrectomy. Care, too, must be observed in determining that the obstruction is actually at the ureteropelvic junction and not, as Hunner has so often emphasized, at some point in the lower ureter.

CHOICE AND TECHNIQUE OF PLASTIC REPAIR

Adequate exposure is essential for the proper execution of pyeloplasty. As a result of the teaching of Hess, a loin incision is made directly down on the twelfth rib which is resected. This incision not only permits excellent exposure of the kidney but affords less chance of injuring nerves supplying the abdominal wall. Exception is made in cases of nephroptosis, in which good exposure can be obtained without removal of the rib.

The proper choice of plastic operation will depend upon whether the hydronephrosis is caused by Type I, II, or III obstruction. The correct classification can sometimes be surmised during preliminary investigation, but can be definitely determined only at operation. The first requirement is, of course, removal of all obstructing fibrous bands and adhesions and division of aberrant vessels—in other words a thorough pyeloureterolysis. This may be all that is necessary to eradicate completely the obstruction to drainage, proving that the lesion is extrinsic (Type I). In per-

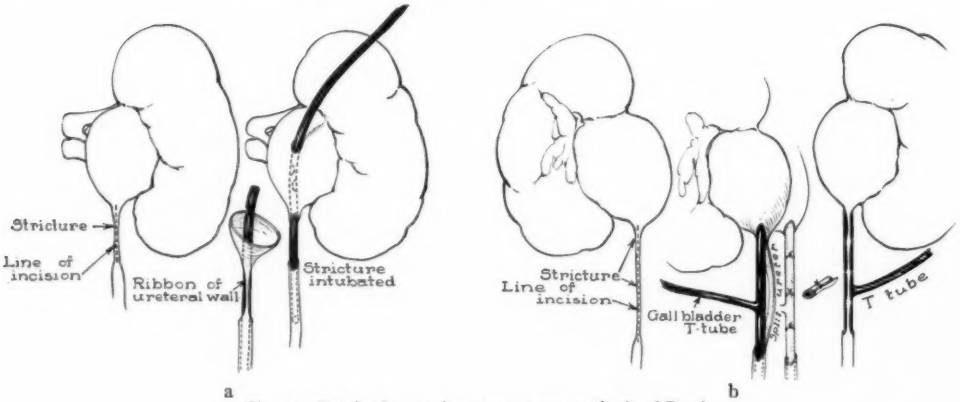


Fig. 10. Intubation pyeloureterostomy methods of Davis.

sonal experience about 50 per cent of cases fall in this category. However, as previously emphasized, the lumen of the ureteropelvic junction should be calibrated before concluding the operation, and ureteral splinting resorted to if there is much peripelvic and periureteral fibrosis with angulation or distortion of the upper ureter.

If the obstruction is intrinsic it will fall in either Type II or III. One then proceeds with an appropriate pyeloplastic operation, as illustrated by Figures 2 to 8, inclusive. For

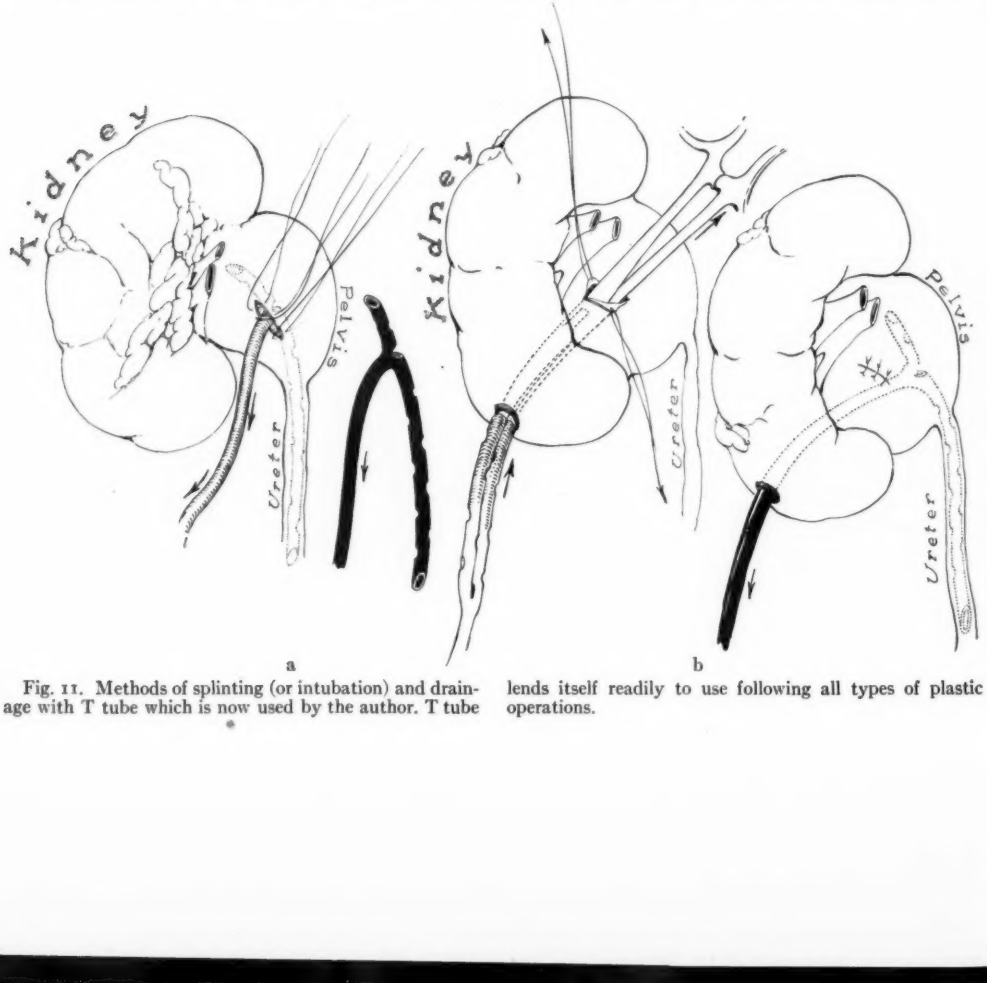


Fig. 11. Methods of splinting (or intubation) and drainage with T tube which is now used by the author. T tube lends itself readily to use following all types of plastic operations.

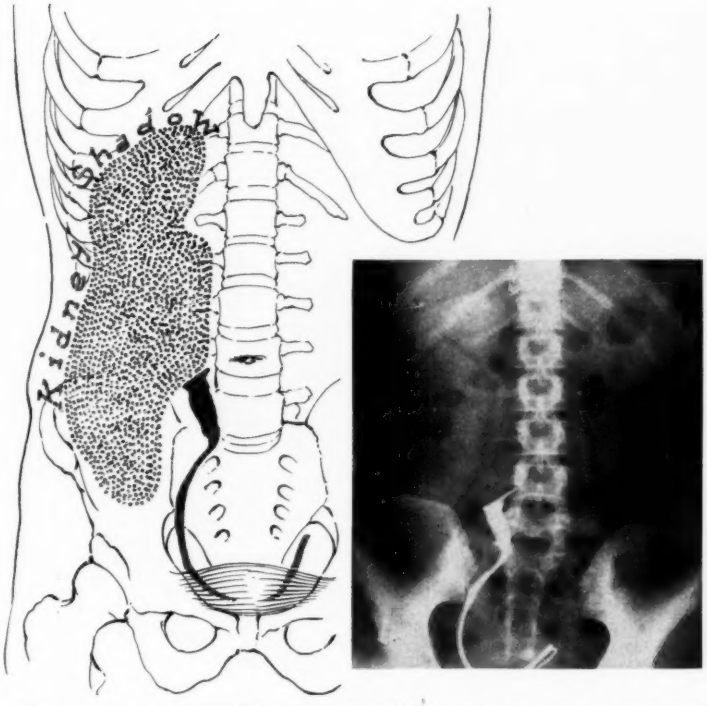
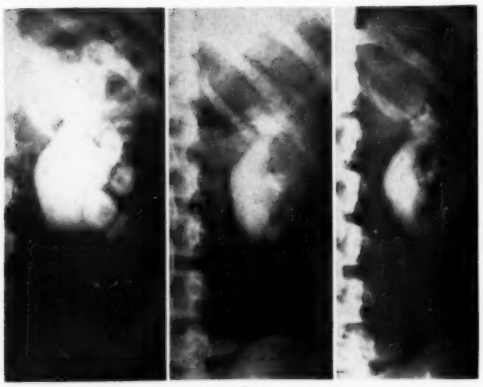


Fig. 12. Case 1. Congenital solitary right kidney. Female, aged 24 years, had chronic infected hydronephrosis of giant proportions, causing externally visible abdominal tumor. On cystoscopic study, it was impossible to pass catheter or force pyelographic medium beyond ureteropelvic junction. Condition of patient was grave due to uremia. At operation kidney was found to be a thin walled, translucent sac with apparently insufficient parenchyma to sustain life. Davis-Rammstedt pyeloplasty was performed with ureteral splinting and nephrostomy drainage with McIver tube. This tube did not maintain its splinting action long, but crawled back into hydronephrotic sac. Nevertheless, patient recovered and reports fair health 1 year later. Large catheters can be passed readily up ureter into kidney pelvis.

Type II obstruction (Fig. 1), consisting of stricture of the ureteropelvic junction, the procedure preferred by the author is the Davis-Rammstedt operation because of its simplicity, ease of execution and excellent end-results (Fig. 6). The pelvis is opened between stay sutures, a Mayo hemostat is pushed down through the ureteropelvic junction, and the jaws are spread gradually until the lumen is more than adequate. Simultaneously, a row of parallel vertical incisions is made about the outside down to the mucosa in order to divide constricting muscle fibers and scar tissue. This step is followed by splinting or intubation (Figs. 9, 10, and 11) to maintain the caliber of the lumen at No. 12 to 14 F. until healing is complete. Other plastic operations such as the Fenger procedure, the Finney pelvioureteroplasty, the ureteropyeloneostomy of Kuester or Lubash, or the Schwyzer-Foley methods may be used with success in Type II obstruction.

For Type III obstruction, involving valve formation with high insertion of the ureter in the pelvis, the original Trendelenburg operation modified (Fig. 2) is still eminently satisfactory. This method was used in the cases illustrated in Figures 12 and 13 with good results. If there is much pouching of the lower pelvis the method of Priestley (Fig. 7) has



a b c

Fig. 13. Case 2. a, Preoperative pyelogram. Congenital solitary left kidney complicated by acute fulminating colon bacillus pyelonephritis. Female, aged 25 years. Inability to maintain catheter drainage and grave condition of patient made emergency operation necessary. Hydronephrosis due to Type III ureteropelvic obstruction was found to be complicated by edematous adhesions and aberrant vein. Pyeloureterolysis with sacrifice of aberrant vessel and Trendelenburg plastic was performed. No sutures were used due to necessity for haste and friable nature of tissues. Ureteral splinting and nephrostomy were maintained for 3 weeks. Complete recovery. b, Pyelogram 6 months, and c, 4 years after operation. Urine now sterile and free from pus cells; intravenous phenolsulfonphthalein, 60 per cent in 1 hour. This case strikingly illustrates the value of pelvioureteral splinting and lends support to Davis' views of the importance of intubated ureterotomy.

merit. In Type III one may also use the reimplantation methods of Kuester or Lubash, or lateral anastomosis procedures as shown in Figures 3, 4, and 6, including that of Foley. In patients with excessively redundant pelvis, radical excision of the pelvis with reanastomosis of the ureter to its lowermost part (Fig. 8) may be practiced. In cases of anomalous artery too large to sacrifice, the procedure of Young (Fig. 5) or ureteropyeloneostomy (Figs. 2 and 7) may be utilized to advantage. In general, No. 00000 chromic catgut mounted on atraumatic needles seems to be the suture of choice in plastic procedures. However, the author regards adequate splinting or intubation as more important in obtaining a good result than the most meticulous suturing.

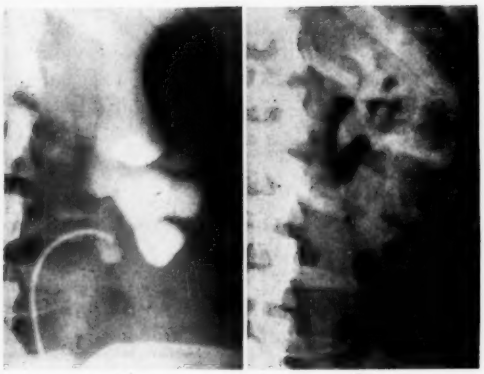
The problem of sacrificing an anomalous vessel requires careful consideration. Anomalous veins may be sacrificed with equanimity; but arteries are terminal without anastomoses, so that a localized area of anemic necrosis results from their loss which may become infected and jeopardize the success of the operation. Shupe reported an interesting exception to this rule in a case in which resection of a slate pencil sized artery extending from the aorta to the lower pole of the kidney did not result in development of an infarct. The lesson to be derived is that it is safer to divide an aberrant vessel to the kidney arising from any source other than the renal artery. Since nephroptosis is a complicating or aggravating factor in a certain percentage of cases of all types, nephropexy should be performed as a part of the operative program when indicated. Renal sympathectomy is occasionally included in the treatment when the obstruction appears to be more dynamic than mechanical in nature, in order to make doubly sure of relieving pain.

URETERAL SPLINTING AND INTUBATION

Consideration of the value of ureteral splinting and intubation with its necessary corollary—nephrostomy, pyelostomy, or ureterostomy drainage— has been purposely reserved until now. In spite of certain dissenting voices, personal experience has led to the conviction that this is the most important single factor in obtaining with certainty a successful end-result in the highly technical field of pyeloplasty. It is doubtless true that splinting or intubation is not always necessary, but general opinion differs from that of Deming who states that splints are unnecessary, and who resorts to drainage only in infected cases. In a communication published in 1939, the author emphasized the value of ureteral splinting following operations on the kidney in which the upper ureter and pelvis are surrounded by dense adhesions causing kinking, narrowing, and distortion. Just previous to that time, failure to utilize splinting in three consecutive cases resulted in the necessity of performing secondary nephrectomy in one. In the other two, ureteral dilators entered the pelvis of the kidney with the greatest difficulty after operation. The following conclusion was reached: it should be axiomatic that the urologist make use of ureteral splinting following operation on all cases of ureteral and renal

a b

Fig. 14. Pyelograms, a, before pyeloplasty, and b, 3 weeks after, showing slight leakage at site of plastic operation.



a b

Fig. 15. Urograms, a, (retrograde) preoperative, and, b, (excretory) 5 years postoperative. Female, aged 25 years, had left calculous hydronephrosis associated with nephroptosis. Pyeloureterolysis, pyelolithotomy, and nephropexy without splinting produced this obviously excellent result.

calculi in which dense adhesions or other types of obstruction to free drainage, either intrinsic or extrinsic, exist about the ureter or pelvis. The author has come to consider this as the most important fundamental surgical principle essential to success in plastic operations for hydronephrosis as well.

The value of the ureteral splint has been emphasized by Peck and later by Harris, Cabot, Moore, Sargent, Priestley, Sharp, and others. More recently, Davis has reported on the value of intubation which he utilized ingeniously in exceedingly difficult cases. His results were so spectacular that his intubation technique has taken precedence at the Jefferson Hospital over all plastic operations on the ureter and ureteropelvic junction (Fig. 10).

The principal methods of splinting, intubation, and drainage are shown in Figures 9, 10, and 11. Personal experience with the Cumming and McIver nephrostomy tubes has been unsatisfactory. One reason is that the splinting portion of the tube which goes down the ureter is not sufficiently rigid, and tends to crawl back into the pelvis (unless the pelvis has been resected), where it coils and completely defeats its purpose. When I visited Deming at Yale in February, 1940, he called the T tube to my attention. Since then I have used it in various ways, as shown in Figures 9 and 11, and have come to depend on it more and more following plastic operations for hydronephrosis, as well as for drainage when required in other types of renal surgery. It can be used in a number of ways with the greatest facility; it can be cut to measure so to speak, and is easily introduced and removed. I wish to draw attention particularly to the fact that one should always cut out a V opposite the stem of the T, not only to render it easily collapsible but also to enable visualization of the opening into the stem. Not infrequently one will find a small flap of overlapping rubber across the opening which can be readily removed so it will not interfere with drainage or irrigation. Multiple openings to facilitate drainage are cut in the T tube as shown in Figure 11. Some writers have expressed objections to nephrostomy drainage because of the danger of infection and secondary hemorrhage. No personal difficulties of this sort have so far been encountered, but for conscientious objectors the T tube lends itself just as readily to pyelostomy or ureterostomy drainage (Figs. 9 and 11). Splinting and drainage should be maintained for a period of 10 days to 3 weeks or more postoperatively depending upon the apparent needs of the individual case.

Proper evaluation of the end-results of plastic repair of ureteropelvic obstructions causing hydronephrosis depends on careful

follow-up studies, including urography, at regular intervals. These examinations have the added advantage of making available early detection and treatment of residual infection or subsequent obstruction. Deming warns against too immediate postoperative ureteral catheterization. A personal case is shown in Figure 14, in which a catheter was passed 3 weeks after operation. The pyelogram reveals some leakage at the site of pyeloplasty, but fortunately no harm came of it. Figure 15 shows the remarkable ability of the kidney to return to normal following removal of obstruction.

SUMMARY

It has been the author's aim in this communication to review the subject of hydronephrosis due to obstruction at the ureteropelvic junction, to describe the three general types of obstruction, and to gather together the principal methods of pyeloplasty in current use. It is hoped that this may serve as a basic reference for the future standardization of plastic procedures.

Experience with pyeloplastic repair suggests the possibility of eliminating the elaborate plastic operations and the delicate suturing they entail in favor of the simpler methods. The value of pyeloureteral splinting and intubation in selected cases is re-emphasized as an insurance against failure. It is even possible that these procedures may supersede to a large extent plastic operations on the ureter and ureteropelvic junction. At the present time we know that pyeloplasty and ureteral splinting or intubation are effective when used conjointly. Future experience will determine their relative rôles, as well as the comparative merits of the various methods of pyeloplasty.

REFERENCES

1. Cabot, H. Discussion of Pilcher (20).
2. Davis, D. M. Urol. Cut. Rev., 1933, 37: 673–674.
3. Idem. Surg. Gyn. Obst., 1943, 76: 513–523.
4. Deming, C. L. J. Urol., Balt., 1943, 50: 420–431.
5. Fenger, C. J. Am. M. Ass., 1894, 22: 335–343.
6. Idem. Collected Works of Christian Fenger. Vol. 2, pp. 687–704. Philadelphia and London: W. B. Saunders Co., 1912.
7. Gibson, T. E. J. Urol., Balt., 1939, 42: 1169–1175.
8. Idem. England J. M., 1940, 222: 910–918.
9. Harris, A. Ann. Surg., 1935, 102: 1050–1058.
10. Henline, R. B., and Menning, J. H. J. Urol., Balt., 1943, 50: 1–24.
11. Hess, Elmer. J. Urol., Balt., 1939, 42: 943–949.
12. Hinman, Frank. Southwest. M., 1942, 26: 357–368.
13. Kuester, E. Ver. deut. Ges. Chir., 1892, 21: 228–232 (pt. 2).
14. Idem. Arch. klin. Chir. 1892, 44: 850–854.
15. Lubash, S. J. Urol., Balt., 1935, 34: 222–229.
16. Lubash, S., and Madrid, A. J. Urol., Balt., 1937, 38: 634–642.
17. Moore, T. D. Am. J. Surg., 1937, 38: 101–115.
18. Ormond, J. K. Am. J. Surg., 1937, 38: 70–79.
19. Peck, C. H. Ann. Surg., 1926, 83: 260–266.
20. Pilcher, F. Proc. Mayo Clin., 1937, 12: 282–283.
21. Priestley, J. T. Surg. Gyn. Obst., 1939, 68: 832–841.
22. Sargent, J. C. J. Urol., Balt., 1937, 38: 680–687.
23. Sharp, R. F. South. M. J., 1943, 36: 549–555.
24. Shupe, T. Tr. Am. Ass. Genitourin. Surgeons, 1942, 35: 15–19.
25. Trendelenburg, F. Cited by Fenger (6), p. 900.
26. Young, H. H. Surg. Clin. N. America, 1936, 16: 1219–1230.

SICKLE FLAP FOR NASAL RECONSTRUCTION

GORDON B. NEW, M.D., F.A.C.S., Rochester, Minnesota

FREQUENTLY one sees a patient on whom a beautiful operation has been done to reconstruct a portion of the nose but the color of the reconstructed part does not match that of the rest of the nose or, if the material for the reconstruction has been used from some other part of the face, the donor area stands out with conspicuous scarring or a discolored skin graft that detracts greatly from the end-result. To be able to obtain material for reconstructing the tip or an ala of the nose from the forehead and at the same time to create very little noticeable defect at the donor site is the advantage of the flap that I am describing.

When a portion of the nose is replaced by a plastic operation, the skin of the new part should blend in size, shape, color, and texture with that of the rest of the nose, but in addition the donor area from which the flap is obtained should not show noticeable scarring or a skin graft that detracts from the result obtained on the reconstructed part. Study and planning of flaps and procedures are necessary to obtain such a result. While many of the minor defects of the ala and tip of the nose may be corrected by sliding flaps or delayed flaps about the nose and cheek with or without the use of a skin graft, the larger defects of the ala and tip require more material than can be obtained in this way. The skin from the forehead has been used for many years for these purposes and is a good match with the skin of the nose. A flap from the cervical region or from the arm as a rule does not blend well with the rest of the nose. The forehead flap used with the supraorbital vessels or the anterior branch of the superficial temporal artery usually leaves considerable scarring on the forehead and also a noticeable patch where the free full thickness skin graft is used to replace the skin used for nasal reconstruction.

In order to avoid this scarring and to obtain a pedicle flap contiguous with the area to be grafted, I have employed a flap in the temple,

From the Section on Laryngology, Oral and Plastic Surgery, Mayo Clinic.

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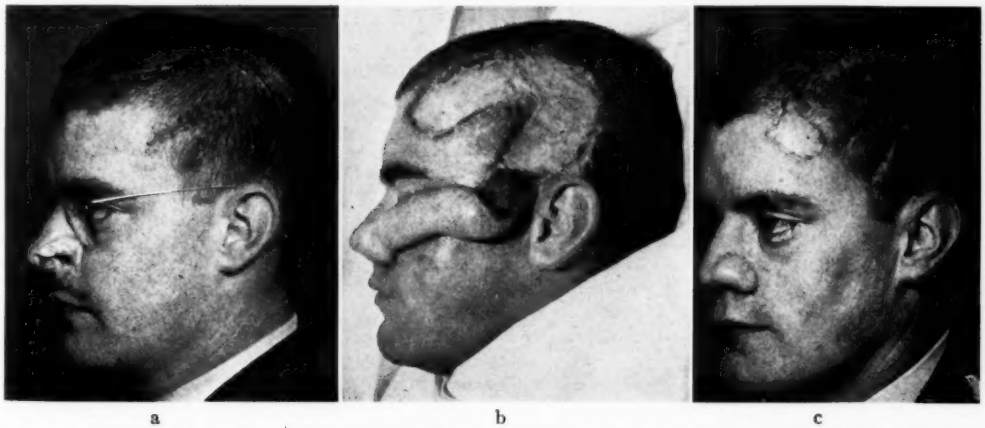

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Fig. 1. a, Postoperative defect of the left ala and tip of the nose 1 year after removal of a postirradiated epithelioma with surgical diathermy. The sickle flap has been elevated and the forehead end has been lined with a skin graft. b, The lined flap has been brought down to the nose. The flap has been tubed by means of petrolatum fine mesh bandage. A skin graft has covered the defect in the scalp and forehead. c, The flap has been replaced. Note the reconstructed part of the nose and the small area of skin graft on the forehead, which can readily be covered with the hair. Photograph made 2 weeks after the last stage of the operation.

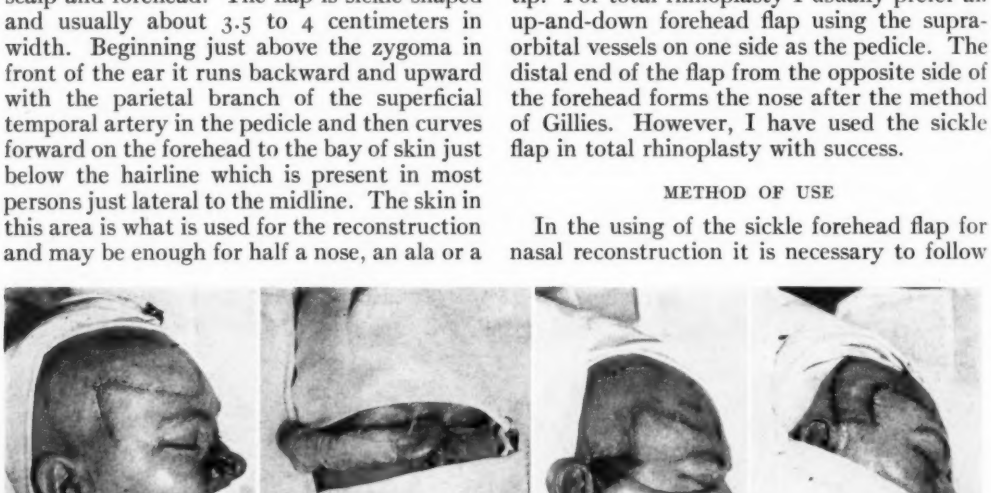
a b c

Fig. 2. a, Postoperative defect of the lower half of the nose 3 years after removal of a postirradiated epithelioma with surgical diathermy. b, The sickle flap has been elevated and delayed and the distal end has been lined with a skin graft. c, The flap has been returned. The small defect where the skin graft is present at the mesial end of the flap may be noted. Sutures have just been removed from the reconstructed nose.

scalp and forehead. The flap is sickle-shaped and usually about 3.5 to 4 centimeters in width. Beginning just above the zygoma in front of the ear it runs backward and upward with the parietal branch of the superficial temporal artery in the pedicle and then curves forward on the forehead to the bay of skin just below the hairline which is present in most persons just lateral to the midline. The skin in this area is what is used for the reconstruction and may be enough for half a nose, an ala or a tip. For total rhinoplasty I usually prefer an up-and-down forehead flap using the supra-orbital vessels on one side as the pedicle. The distal end of the flap from the opposite side of the forehead forms the nose after the method of Gillies. However, I have used the sickle flap in total rhinoplasty with success.

METHOD OF USE

In the using of the sickle forehead flap for nasal reconstruction it is necessary to follow



a b c d

Fig. 3. a, The defect in the right side of the nose and cheek and inner canthus may be noted. There is a loss of the right half of the nose and of a portion of the bridge and of the cheek. A sickle flap has been elevated and the distal end has been lined with a skin graft to line the part of the flap that will reconstruct the ala and right side of the nose. b, The flap has been brought down to the nose. That part which is to reconstruct the nose is lined with a skin graft. The flap has been tubed by means of fine mesh gauze bandage. c, The defect in the forehead and scalp has been skin grafted. The flap has been tubed by means of fine mesh gauze bandage. Before being replaced, flap is cut half way across and then resutured at the point to be sutured to cheek in order to insure the blood supply on the new skin over the nose. d, The flap has been replaced and stretched so that it is not necessary to leave more than a small skin graft on the forehead below the hairline. The reconstructed portion of the nose has been sutured to the cheek.

the delayed flap technique in order to insure the blood supply. Careful planning is essential so that material obtained will be of the right size and shape and free from hairs. The area to be employed is marked out with blue pencil on the forehead just lateral to the midline and just below the hairline. Then the hair is shaved and a flap is marked out with indelible pencil, adhesive tape or gauze bandage being used as a pattern so that the flap is of sufficient length at the time of operation. One must remember that the lower margin of the flap determines its length, so that it should be made long enough. The flap is elevated, both pedicles being left intact. At this time or at a second stage the mesial end of the flap may be lined with a shaved skin graft as in the making of an ala, so that it will have skin on both sides. The forehead end of the pedicle is cut across at its subsequent stage to the skin grafting of the lining and then at a later stage the flap is brought down to the defect in the nose. It may be advisable to make one complete elevation of the flap before bringing it down in order to insure the blood supply.

If the flap is to be employed to reconstruct the lower half of the nose including the tip and columella and has to be folded on itself, I feel that a better shaped nose is obtained if the bringing down of the flap is delayed until 3 months after the flap has been prepared. In this way when the flap is brought down, it is very thin and folds readily; it makes a better shaped nose than if it has been elevated and brought down when it is quite thick and difficult to fold. When the flap is brought down, it is an open flap and is converted into a closed one by wrapping with 2 inch (5 cm.) gauze bandage. This also protects the eye for 2 or 3 days from the hair bearing flap until it sags down on the cheek. At the time of the operation the raw surface on the forehead is completely covered with a shaved graft. After the flap has been in place for 2 weeks the point in the flap that will form the distal margin of the reconstructed part is cut half way across and sutured and then a week later it is completely cut across and the pedicle and distal portion of the flap are replaced on the forehead after removal of the skin graft. In many cases it is possible to stretch the flap so that the entire skin graft may be replaced with the flap, thus leaving no skin graft visible at the lower margin of the hairline. This lowers the hairline a little but in most cases not enough to be noticeable and I feel that it is a distinct advantage. If it is impossible to remove all the skin graft, the lower and mesial portions of it which remain may be excised at a secondary operation.

Fig. 4. a, left, Defect following removal of postirradiated squamous cell epithelioma of the nose. This was replaced with a lined sickle flap from the scalp and the forehead. b, It was possible to stretch the replaced flap so that the small area of the skin graft that was left was excised 3 months later without leaving any grafted area on the forehead. The skin of the reconstructed portion of the nose matches in color and texture with that of the rest of the nose.

Figures 1, 2, 3, and 4 illustrate the various steps in the procedure.

REFERENCE

1. Gillies. Quoted by Kilner, T. P. in Maingot, Rodney: Post-graduate Surgery. Vol. 3, chap. 6, pp. 3762–3788. New York: D. Appleton-Century Co., Inc., 1937.

TUMORS OF THE SUBCUTANEOUS TISSUE AND FASCIA

With Special Reference to Fibrosarcoma—A Clinical Study

DAVID A. WILSON, M.D., Durham, North Carolina

A REVIEW of tumors of the subcutaneous tissue and fascia seen in the Surgical Out Patient Department and in the Surgical Pathology Laboratory of Duke Hospital from 1931 to 1941 was undertaken in an attempt to determine criteria for the early diagnosis and to evaluate more clearly the treatment of fibrosarcoma. This study included all the tumors of the subcutaneous tissue and fascia, benign and malignant, seen during that period, totalling 871 cases out of 80,000 surgical specimens studied.

The ratio of benign to malignant tumors was 8 to 1. Despite this relative frequency of malignant tumors the diagnosis is frequently established only after the tumor attains considerable size or the overlying skin becomes ulcerated. Several factors tend to obscure the early diagnosis of fibrosarcoma, foremost of which is the slow growth and innocent character of many of the tumors, and their gross and microscopic similarity to benign lesions. Histologically fibrous tissue tumors may range from simple fibromas to very cellular fibrosarcomas. Occasionally a clear cut differentiation between the two is impossible because of the lack of definite criteria. For this reason it has been said that every relatively cellular fibroma, no matter how casual its clinical or histological appearance, should be considered malignant until its subsequent behavior is established. In these borderline cases the choice of treatment depends upon the individual surgeon's experience, influenced by the clinical history, the x-ray findings, the size, location, rate of growth, and the presence of other fibrous tumors over the body.

With these features in mind a study was made for comparison of benign and malignant tumors with emphasis on those cases classified as fibromas and fibrosarcomas in which a mistaken diagnosis is apt to occur. The study did not include lymphosarcoma, metastatic carcinoma, melanosarcoma, or the rarer tumors of subcutaneous and fascial origin.

From the Department of Surgery and Pathological Laboratory, Duke University School of Medicine and Duke Hospital.

INCIDENCE

Fibrosarcoma occurred 111 times or 1 in 2400 patients examined. Meyerding, Broders, and Hargrave reported the incidence of fibrosarcoma of the extremities to be 1 in 4,000 patients seen at the Mayo Clinic. Bick (3) reported 84 fibroplastic tumors from the Hospital for Joint Disease, 1930–1936, representing 22 per cent of all tumors seen and 41 per cent of all soft tissue tumors of the extremities.

The relative incidence of the various connective tissue tumors in our series was as follows: Of 871 cases, 111 were fibrosarcomas, 142 fibromas[1], 358 lipomas, 142 hemangiomas, 17 lymphangiomas, 39 angioendotheliomas, 31 neurofibromas, and 31 neurilemmomas.

SEX

Fibrosarcomas occurred 68 times in the male and 43 times in the female, a ratio of 1.6 to 1. The preponderance of fibrosarcoma in males as compared to females is evident in other authors' series. Meyerding, Broders, and Hargrave reported a ratio of 2 males to 1 female with fibrosarcoma of the extremities. Quick and Cutler reported a ratio of 1.5 males to 1 female.

This is in distinct contrast with the occurrence of benign tumors, which occurred more often in females or in equal sex distribution (Table I).

RACE

Fibrosarcomas occurred 39 times in negro and 82 times in white patients. The incidence was slightly higher in the white race than in the colored race when compared to the ratio of white patients (62 per cent) and colored patients (38 per cent) seen in the Clinic annually (Table II).

[1]Keloids not included.

TABLE I.—SEX INCIDENCE OF FIBROSARCOMAS AND BENIGN TUMORS OF THE SUBCUTANEOUS TISSUE AND FASCIA

	Males	Females
Fibrosarcomas	68	43
*Fibromas	66	76
Lipomas	133	220
Hemangiomas	56	82
Lymphangiomas	7	12
Angioendotheliomas	20	19
Neurofibromas	18	13
Neurilemmomas	11	20

*Keloids excluded

TABLE II.—RACE INCIDENCE OF FIBROSARCOMAS AND BENIGN TUMORS OF THE SUBCUTANEOUS TISSUE AND FASCIA

	Colored	White
Fibrosarcomas	39	82
Fibromas	44	98
Lipomas	88	270
Hemangiomas	12	126
Lymphangiomas	6	13
Angioendotheliomas	6	33
Neurofibromas	13	18
Neurilemmomas	3	29

AGE

The age incidence of fibrosarcomas in our series closely paralleled the age incidence of benign fibromas (Table III). Although usually stated as being a disease of past middle life they have been reported as occurring at all ages. In our series an almost equal distribution occurred between the ages 10 and 70, the average age being 36.4. The youngest was 2 years of age and the oldest 80. Quick and Cutler reported an equal distribution between ages 30 and 60. Meyerding, Broders, and Hargrave, in their series of 152 cases with fibrosarcoma of the extremities, found the average age incidence to be 43.2. Hudson described a case of intrauterine fibrosarcoma of the foot. Table III shows the age distribution of fibrosarcomas as compared to other benign tumors of the subcutaneous tissue and fascia.

RELATION OF TRAUMA

There is evidence to support the view that trauma may be a factor in the formation and acceleration of many benign subcutaneous tissue tumors. This is especially evident in studies of fibromas arising from the abdominal wall in operative scars (Penick) and on the hands and feet. Mankin, in his studies of 629 neoplasms of the anterior abdominal wall, reported 423 fibromas and 155 fibrosarcomas. Of these 629, 544 were women, 90 per cent of whom were parous, and in 62 per cent of whom a definite relationship between pregnancy and origin or acceleration of growth was found to exist. Waugh in 55 cases of fibroma of the abdominal wall found a close association with pregnancy in 25 cases, trauma in 6 cases, and surgical incisions in 15 cases.

The relationship of trauma to the formation or acceleration of fibrosarcoma is doubtful. Occasionally a fibrosarcoma occurs in an area subjected to repeated trauma (Quick and Cutler). Rarely do they occur in old burn scars or in indolent ulcers (Fleming and Rezek, Glasser). Single episodes of trauma are frequently associated by patients with the appearance of a fibrosarcoma. In our series 3 patients gave a history of a single episode of trauma followed in a short period of time by a fibrosarcoma. Not infrequently patients gave a history of a single episode of trauma followed by edema, discoloration, and a small subcutaneous nodule which persisted for years and then began to grow rapidly following another slight injury or with no subsequent trauma. Biopsy would reveal fibrosarcoma. Meyerding, Broders, and Hargrave reported 17 out of 152 cases of fibrosarcoma which were associated with trauma. Quick and Cutler reported 14 of 72 cases with a history of trauma. Case reports of fibrosarcomas occurring after a single episode of trauma are becoming increasingly more numerous (Blake and Bradford, Zieman, O'Brien).

A simple fibroma may occasionally be the site of origin of a fibrosarcoma. (Fahr, Geschickter and Lewis). Unfortunately, one rarely has more evidence than the patient's history to corroborate this fact and, from a histological standpoint, it may be difficult to differentiate between a low grade fibrosarcoma and a simple fibroma (Fig. 1). Case 3 offers an illustration.

W. J., a 39 year old white man was first seen September, 1931, with a tumor of the left hand measuring 5 by 4.5 centimeters. He gave a history of gradual enlargement over a period of 30 years with some recent increase in growth. Local excision was performed September 29, 1931. The pathological report was simple fibroma with calcification. Three months later the patient noted the recurrence of a

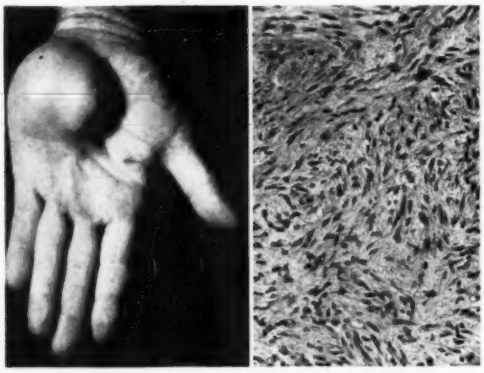


Fig. 1. Fibrosarcoma of the hand in a 39 year old white man with a history of gradual enlargement over a period of 30 years. Photomicrograph shows similarity to simple fibroma.

small nodule in the operative site. This grew rapidly and in March, 1932, wide local excision was performed and the defect was filled with a full thickness graft. The tumor again recurred in 3 months and in October, 1932, the left hand was amputated. The patient died in 1934 from pulmonary metastases.

GROSS CHARACTERISTICS

Primary fibrosarcoma arises most frequently in the subcutaneous tissue and fascia and less frequently in the tendons, dermis, and muscle. Fibrosarcomas have been reported arising primarily in the heart (16, 23, 37), kidney (36), epididymis (28), prostate (33), adrenal gland (12), stomach (9), ileum (25), lung (8), bronchus (6), brain (10), and dura (7, 31).

Fibrosarcoma appears to have a predilection for certain topographical areas of the body, occurring more frequently around the upper thigh and shoulder region and to a lesser extent around the knee and elbow (Table IV). The reason for this is not evident. The tumors are usually densely adherent to the fascial septa extending deep between the muscle groups but occasionally completely encased within a single muscle (Fig. 2).

Rarely can a definite nerve origin be demonstrated although nerves and blood vessels running in the fascial septa may be included within the growth. All too frequently it is impossible to determine the specific site of origin (Fig. 3).

The tumors are usually single but occasionally multiple nodules may be found in the subcutaneous tissue. These probably represent metastatic lesions. Fibrosarcomas are usually rounded or lobulated and vary greatly in consistency from a stony hard fibroid-like texture to a soft lipomatous consistency. The gross character reflects the microscopic appearance, being dependent upon the relative cellularity of the tissue, the amount of mucoid and fibrous intercellular substance, edema, and hemorrhage. On section the acellular fibrous growths cut with a hard, rubbery sensation and reveal a fasciculated arrangement. The more cellular tumors present a homogenous cross section divided into lobules by fibrous septa and numerous blood vessels.

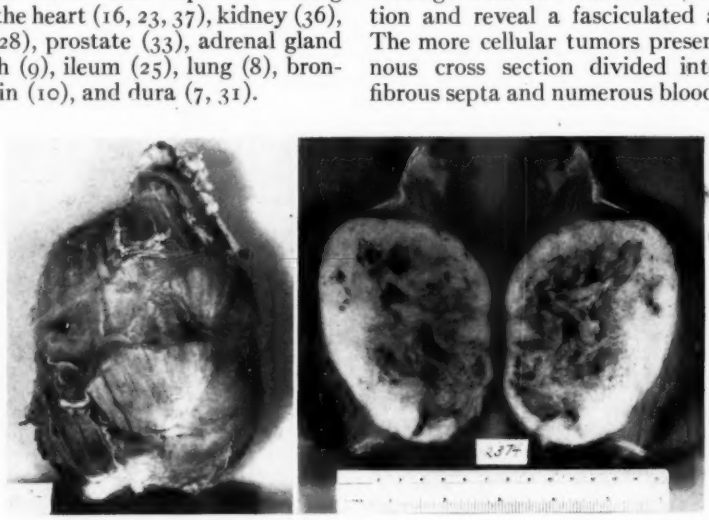


Fig. 2. A fibrosarcoma encased within a single flexor muscle removed from the thigh of a 27 year old white man.

Fig. 3. Fibrosarcoma of the foot in a 44 year old colored female treated by amputation. Case illustrates difficulty in determining specific origin.

Fibrosarcomas grow expansively and in a major portion of cases appear to be encapsulated (Fig. 4). Invasion of the surrounding tissue is, however, the rule and local recurrences result when excision within the false capsule is attempted. The tumor may invade and destroy the adjacent bone or the skin with resulting ulceration, secondary infection, hemorrhage, and anemia. Extension into vessels accounts for frequent distant metastases (13).

The gross measurements of fibrous tissue tumors would appear to aid greatly in the diagnosis of border line cases when the microscopic picture is difficult to interpret. In our series 90 per cent of fibrosarcomas measured over 5 centimeters in diameter when the patients first presented themselves for examination, whereas 85 per cent of fibromas measured under 3 centimeters. Only 13 of the 142 fibromas measured over 5 centimeters in size, and of these 2 recurred and were later reclassified as fibrosarcomas, 3 were fibromyxomas, and 5 desmoid tumors of the abdominal wall. Only 3 of 31 neurilemmomas measured over 4 centimeters in size.

MICROSCOPIC CHARACTERISTICS

Fibrosarcomas grade from very cellular anaplastic types to fibrogenic tumors difficult to differentiate from fibromas. In most cases the diagnosis is easily established from the microscopic structure and the presence of mitotic figures, but in an occasional case the diagnosis is determined only by the subsequent clinical course (Fig. 1).

Fibrosarcomas have been classified as to their growth potentialities by Quick and Cutler, Geschickter and Lewis, Broders, Hargrave and Meyerding. Classification is based upon the differentiation of the cells as manifested by their ability to produce fibrillar intercellular substance by the number of mitotic figures and giant cells and by the relative cellularity and anaplasia of the tissue itself. Quick and Cutler designated as grade I those sarcomas made up of spindle cells lying in a dense stroma of intercellular substance; grade II as those composed of large spindle cells with little intercellular substance, and grade III as those made up of small spindle cells arranged in a fasciculi arrangement or large irregularly shaped cells growing diffusely with little or no

Fig. 4, left. Fibrosarcoma of the left shoulder in a 36 year old colored man, showing characteristic growth.

Fig. 5. Metastases to the inguinal lymph nodes of a 72 year old white man, following amputation for fibrosarcoma of the leg.

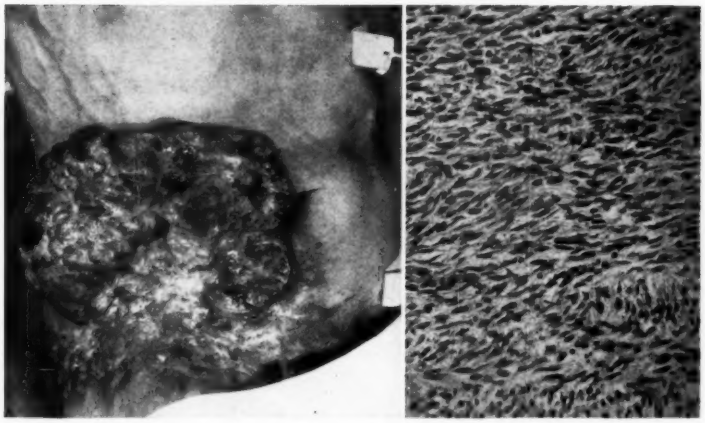


Fig. 6. Fibrosarcoma of the abdominal wall of 32 years' duration in a 57 year old white man. Patient died of pulmonary metastases.

intercellular substance. Geschickter and Lewis made only 2 divisions: differentiated and undifferentiated. Stewart and Copeland; French; and Broders, Hargrave, and Meyerding graded essentially according to the system of Quick and Cutler. In the series of Stewart and Copeland 16 were graded I, 36 were graded II, and 21 were graded III. Broders, Hargrave, and Meyerding subdivided fibrosarcomas microscopically into four grades. Twenty-four fibrous tumors were classified as grade I, 35 fibrocellular tumors as grade II, 23 cellular afibrous tumors as grade III and 70 cellular and anaplastic tumors as grade IV. The relative proportion of cells to fibrillar intercellular substance is undoubtedly the best single criterion for estimating the growth potentialities of fibrosarcomas. The number of mitotic figures is a less reliable index especially in the cellular group. All highly cellular fibrogenic sarcomas have been found to be extremely malignant irrespective of the number of mitotic figures (5). The presence of giant cells is indicative of a higher degree of malignancy (34).

Fig. 7. Fibrosarcoma of the shoulder well since interscapulothoracic amputation in 1938.

With these criteria as a basis for evaluation the fibrosarcomas in our series were carefully reviewed and classified according to the system of Broders, Hargrave, and Meyerding (Table V). A close parallel was found to exist between the clinical prognosis and the histological character of the sarcoma. This also appeared to hold true with respect to the tendency of the fibrosarcoma to metastasize early. Of the 11 patients who had distant metastases when first examined 9 were of grade IV. Contrary to common belief recurrences following local excision were not of a higher grade of malignancy than the primary tumor. In most cases the histological character of the sarcoma was reproduced with successive recurrences. Occasionally a higher grade was encountered.

METASTASES

Metastases in fibrosarcoma usually occur late by way of the blood stream. The most

TABLE III.—AGE INCIDENCE OF FIBROSARCOMAS AND BENIGN TUMORS OF THE SUBCUTANEOUS TISSUE AND FASCIA

Age in years	Under 1	1–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80
Fibrosarcomas	0	8	19	19	22	10	16	13	4
Fibromas	5	13	16	28	27	36	12	5	0
Lipomas	1	7	9	53	85	94	69	33	7
Neurofibromas	0	2	6	13	6	3	1	0	0
Neurilemmomas	0	0	4	5	3	9	3	7	0
Hemangiomas	25	24	18	30	13	16	7	6	3
Lymphangiomas	5	6	3	2	1	0	0	0	0
Angioendotheliomas	6	5	5	4	5	8	4	1	1

frequent site of spread is to the lungs. The regional lymph nodes may be involved (Fig. 5), as in 4 of our cases (Warren and Sommer).

Occasionally metastases are found in the subcutaneous tissues before pulmonary metastases become evident. This was observed in one case of fibrosarcoma of the leg with lymph node metastases. Here the metastases probably represented cells arrested in the lymphatic channels draining the primary site. In 2 other cases multiple subcutaneous tumors occurred in widely separated areas undoubtedly as a result of blood stream spread similar to that seen in melanosarcoma.

DIFFERENTIAL DIAGNOSIS

From a surgical viewpoint differential diagnosis between fibrosarcoma and benign subcutaneous tumors may be difficult. In the major portion of cases, however, the diagnosis can be made by examination alone. The hard fibrosarcomas grossly resemble simple fibromas and fibrosing angiomas. The semihard tumors must be differentiated from neurofibromas and neurilemmomas while the soft edematous sarcomas are often confused with benign lipomas.

Fibrosarcomas may be differentiated from fibromas by their size, by their more rapid expansile type of growth; by their characteristic location about the thigh, shoulder, knee and elbow, and by their tendency to invade and destroy skin and bone. Fibrosarcomas arising in the abdominal wall are especially hard to differentiate grossly from desmoid tumors.

Any small subcutaneous nodule which has persisted for years and then begins to grow rapidly should be suspected of malignant change.

Neurilemmomas, like fibrosarcomas, are usually solitary. They are of semisolid consistency and freely movable except along the axis of the nerve sheath from which they arise. They are well encapsulated; invasion of surrounding structures and ulceration of the

TABLE IV.—TOPOGRAPHICAL LOCATION OF FIBROSARCOMAS AND BENIGN TUMORS OF THE SUBCUTANEOUS TISSUE AND FASCIA

	Head and neck	Arm and shoulder	Elbow and forearm	Hands and feet	Body	Thigh	Knee and legs	Genitalia
Fibrosarcomas	9	18	6	7	abd. 7 chest 6 back 6	35	16	1
Fibromas	27	15	3	27	30	14	25	1
Lipomas	51	96	14	8	abd. 23 chest 31 back 52	61	14	8
Hemangiomas	69	6	2	16	30	2	12	5
Lymphangiomas	11	0	1	2	1	2	0	0
Angioendotheliomas	18	6	1	5	4	4	1	0
Neurinomas	13	9	2	4	0	0	2	1
Neurofibromas	10	1	1	4	10	3	2	0

TABLE V.—RESULTS OF TREATMENT

	Clinically cured	Living with disease*	Dead	Total
Grade I				
Local excision	10	1		11
Amputation	2			2
Biopsy and x-ray			1	1
Total	12	1	1	14 (12.6%)
Grade II				
Local excision	7	3	8	18
Amputation	1	1		2
Biopsy and x-ray		1	6	7
Total	8	5	14	27 (24.3%)
Grade III				
Local excision	4	1	7	12
Amputation	1		2	3
Biopsy and x-ray		1	3	4
Total	5	2	12	19 (17.1%)
Grade IV				
Local excision	5	1	22	28
Amputation	3		7	10
Biopsy and x-ray			13	13
Total	8	1	42	51 (46%)
Total	33 (29.7%)	9 (8.1%)	69 (62.2%)	111 (100%)

*Included in this group are cases treated for recurrences since 1941.

overlying skin is absent. Growth is slower and rarely do they reach the dimensions of a fibrosarcoma of the same duration. Because of their origin from the nerve sheath, pressure on the tumor frequently causes pain to radiate along the distribution of the nerve. They occur more commonly in the neck from the brachial plexus and along the medial aspect of the arm from the ulnar and median nerves. Fibrosarcomas rarely occur at these sites.

Soft fibrosarcomas are frequently confused with lipomas which they closely resemble in consistency, size, and expansile type of growth. Lipomas are more apt to occur in those areas of the body where adipose tissue is normally concentrated and as they increase in size frequently become pedunculated. Lipomas in unusual sites are more frequently misdiagnosed as fibrosarcoma than the reverse. Aspiration biopsy has proved an aid in these cases.

CLINICAL ASPECTS AND TREATMENT

The high mortality rate in patients with fibrosarcoma speaks for the difficulties in the management of this malignant tumor. These difficulties are due in part to the wide variation in rate of growth, the invasive character of the tumor, and the tendency to blood stream metastases. In our series of 111 cases, 11 had pulmonary metastases when first examined and 33 had had previous local exicsions. The duration of symptoms varied from 1 month to 32 years (Fig. 6). The average duration was 1 to 3 years with local recurrence showing up as late as 15 years following the primary excision.

Of utmost importance is the early recognition of the malignant nature of the tumors and wide surgical excision. It is a general feeling that amputation in fibrosarcoma of the extremities will more often effect a cure than local excision. This is probably true; however, if amputation was generally adopted for fibrosarcomas of the extremities many limbs would be unnecessarily sacrificed (Table V). Amputation has usually been reserved for those cases in which local excision has failed or has not been applicable due to the extensiveness of

the growth. The decision between amputation and local excision should be based upon a careful evaluation of the clinical history, the speed of growth, the size, location, and the histological character of the tumor. Biopsy or wide local excision should be performed and histological sections studied before amputation is advised. If biopsy is performed at the time of amputation, the same care should be taken to avoid transplanting tumor cells into an uninvolved area, as is taken in excising carcinoma. Local recurrences may result from failure to observe this precaution (Harrell and Valk). Highly malignant tumors of the extremities and those arising in or invading the periosteum should be treated by amputation. Acellular, slow growing tumors arising in muscle and the musculofascial septa may be treated by wide local excision. Those arising in the dermis and subcutaneous tissue are preferably treated by local excision. Occasionally fibrosarcomas of the shoulder or thigh require interscapulothoracic or ileoabdominal amputation to secure a satisfactory margin of safety (24) (Fig. 7).

X-ray therapy in the treatment of fibrosarcoma is without appreciable value. Growth in an occasional case appears to be retarded but no cures have been reported. Patients should be warned of possible damage to normal surrounding structures and of retarded epiphyseal growth in young individuals (Doub) (14).

Radical dissection of the regional lymph nodes was performed in a few selected cases but the series is too small to draw any conclusions as to the therapeutic value.

RESULTS OF TREATMENT

In our series of 111 cases 33 cases, or 29.7 per cent, were listed as clinically cured. Of these 33 cases 3 have been well over 11 years, 17 have been well 7 to 10 years, 10 have been well 6 years, 2 have been well 5 years, and 1 has been well 4 years (Table V). Eleven of these had had previous local excisions. Of 14 classed as grade I, 12, or 85 per cent, are well; of 27 classed as grade II 8, or 29.6 per cent, are well; of 19 classed as grade III 5, or 26.3 per cent, are well; of 51 classed as grade IV 8, or 15.7 per cent, are well.

The mortality rate was 62.2 per cent; 8.1 per cent are still living with the disease or have had recent local recurrences treated.

The results with local excisions in grades I and II were satisfactory, but amputation if possible would appear to be indicated in grades III and IV.

In 25, or 22.5 per cent, only biopsy was performed and x-ray therapy given. Of these 25, 11 had pulmonary metastases, 3 had subcutaneous metastases, and 3 had lymph node metastases when first examined. Two are still living, one 8 years with a fibrosarcoma of the thigh and one 5 years with a fibrosarcoma of the jaw following x-ray therapy.

SUMMARY

Eight hundred and seventy-one soft tissue tumors occurring in 80,000 surgical specimens examined during the years 1931 to 1941 were classified as to sex, race, age, anatomical distribution, and size. There were 111 fibrosarcomas, 142 fibromas, 358 lipomas, 142 hemangiomas, 17 lymphangiomas, 39 angioendotheliomas, 31 neurofibromas, and 31 neurilemmomas. The ratio of benign to malignant tumors was 8 to 1.

Fibrosarcomas occurred 68 times in males and 43 times in females, a ratio of 1.6 to 1. This was in contrast to the benign tumors which occurred more frequently in females or showed an equal sex distribution (Table I).

The race distribution showed a slightly higher incidence in white than colored patients (Table II).

Fibrosarcomas occurred with almost equal frequency between the ages of 10 and 70, being slightly higher between the ages of 30 and 40. The average age incidence was 36.4. The average age incidence for fibromas was 32.1 years and for lipomas 42.3 years.

Fibrosarcomas occurred more frequently about the thigh and shoulder regions. Fibromas occurred more frequently around the head, hands, and feet and legs, and lipomas showed a higher incidence on the body (Table IV).

The 111 fibrosarcomas were classified according to the relative proportion of cells to fibrillar intercellular substance, the number of mitotic figures, the number of giant cells, and

the regularity or anaplasia of the cells. The histological character was found to be an accurate index of the growth potentialities and an aid to prognosis and treatment.

The mortality rate was 62.2 per cent; 29.7 per cent were well and 8.1 per cent were still living with the disease.

REFERENCES

1. Batts, M., Jr. Arch Surg., 1941, 42: 566.
2. Bick, E. M. Ann. Surg., 1935, 101: 759.
3. Idem. Arch. Surg., 1937, 35: 841.
4. Blake, J. M., and Bradford, J. K. J. Thorac. Surg. 1943, 12: 368.
5. Broders, A. C., Hargrave, R., and Meyerding, H. W. Surg. Gyn. Obst., 1939, 69: 267.
6. Case Records of the Massachusetts General Hospital. Case 24202. N. England J. M., 1938, 218: 843.
7. Idem. Case 24312. N. England J. M., 1938, 219: 169.
8. Idem. Case 24472. N. England J. M., 1938, 219: 854.
9. Idem. Case 27272. N. England J. M., 1941, 225: 38.
10. Cattrell, L. Arch. Path., 1939, 27: 895.
11. Collins, N. C., and Auspach, W. E. Am. J. Cancer, 1940, 40: 465.
12. Cran, B. S. Brit. M. J., 1933, 2: 1018.
13. Davis, G. G. Arch. Surg., 1935, 31: 531.
14. Doub, H. P. Radiology, 1938, 30: 122.
15. Fahr, E. Derm. Wschr., 1934, 99: 1231.
16. Fidler, R. S., Kissane, R. W., and Koons, R. N. Am. Heart J., 1937, 13: 736.
17. Fleming, R. M., and Rezek, P. Am. J. Surg., 1941, 54: 457.
18. French, R. W. N. England J. M., 1932, 206: 393.
19. Geschickter, C. F., and Lewis, D. Am. J. Cancer, 1935, 25: 630.
20. Glasser, S. T. Am. J. Surg., 1939, 43: 776.
21. Harrell, G. T., and de T. Valk, A. Ann. Surg., 1940, 111: 285.
22. Hudson, O. C. Am. J. Cancer, 1936, 26: 568.
23. Jackson, M. N., and Jackson, J. N. Lancet, 1930, 2: 740.
24. Levinthal, D. H., and Grossman, A. Surg. Gyn. Obst., 1939, 69: 234.
25. Mahaffey, H. Kentucky M. J., 1940, 38: 567.
26. Mankin, Z. W. Arch. klin. Chir., 1932, 169: 688.
27. Meyerding, H. W., Broders, A. C., and Hargrave, R. L. Surg. Gyn. Obst., 1936, 62: 1010.
28. O'Brien, G. O. J. Urol., Balt., 1942, 47: 311.
29. Penick, R. M. Internat. S. Digest, 1937, 23: 323.
30. Quick, D., and Cutler, M. Am. Surg., 1927, 86: 810.
31. Russell, W. O., and Sachs, E. Arch. Path., 1942, 34: 240.
32. Stewart, F. W., and Copeland, M. Am. J. Cancer, 1931, 15: 1235.
33. Townsend, T. M., and Kobisk, O. A. N. York State J. M., 1936, 36: 499.
34. Warren, S., and Sommer, G. N., Jr. Arch. Surg., 1936, 33: 425.
35. Waugh, J. M. Am. J. Surg., 1940, 50: 694.
36. Weisel, W., and Dockerty, M. B. J. Urol., Balt., 1942, 47: 410.
37. Willius, F. A. Proc. Mayo Clin., 1938, 13: 331.
38. Zieman, A. Surgery, 1941, 9: 675.

ARTERIAL EMBOLISM

A Simplified Technique for the Removal of a Saddle Embolus at the Bifurcation of the Aorta with the Report of a Successful Case

ROBERT R. LINTON, M.D., F.A.C.S., Boston, Massachusetts

ARTERIAL embolectomy is one of the real emergency operations in surgery. In order to restore the arterial circulation the embolus must be removed within a few hours of the time of embolism before secondary thrombosis has developed distal to the embolus. A cold painful cadaveric appearing extremity, without motor function or sensation, becomes again within a few minutes a living part of the body and gangrene necessitating amputation is prevented.

The bifurcation of the aorta is not an uncommon site for the lodgment of an embolus. Pearse, in 1933, found 34 cases in a review of 282 reported embolectomies. Many patients have developed bilateral gangrene because either this site has been considered inaccessible to the direct approach for embolectomy, or it was felt that the patient, due to his cardiac condition, would not withstand the operation necessary to expose the aorta. McClure and Harkins, in an excellent review of the literature on arterial embolism, found and tabulated 19 cases of successful aortic embolectomy by 16 surgeons. The first one was reported by Bauer in 1913. Murray reported the cases of 4 patients operated upon by him, the largest single group.

The purpose of this paper is to discuss the principles of embolectomy, to report another successful embolectomy at the bifurcation of the aorta by a transperitoneal exposure, and to describe a new method of arterial control and technique for the removal of the embolus, which has been found to facilitate greatly the operative procedure.

PRINCIPLES OF EMBOLECTOMY

Embolectomy is not a difficult operative procedure provided certain principles are followed. Any surgeon should be able to perform a successful embolectomy if he has mastered the art of meticulous atraumatic surgery. The adherence to the following six principles is considered of the greatest importance if a successful result is to be obtained. The first principle is that an embolectomy must be carried out at the earliest possible time following the lodgment of the embolus. It is one of the real emergency operations in surgery, since a matter of a few hours may mean the difference between a viable extremity and gangrene. Too often the physician who first sees the patient does not realize this, and it is not until the extremity is obviously gangrenous that he refers the patient to a surgeon. By then it is impossible to save the limb because of the formation of a secondary thrombus filling the arterial tree distal to the site of the embolism. This condition may develop as early as 9 hours from the time of embolism as reported by Linton.

The second principle is that a direct and adequate exposure of the artery at the site of embolism should be obtained. The most gentle manipulation of the involved artery is necessary if the embolectomy is to be successful, since rough handling and poor technique due to inadequate exposure may produce irreparable damage with secondary thrombosis. It is impossible to determine by a review of the literature the percentage of successful results with any one method of exposure, since unsuccessful cases frequently are not reported. The operative approach in the 19 successful cases reported by McClure and Harkins was transperitoneal in 5 cases, extraperitoneal in 5, and retrograde in 7; in 4 of the latter group retrograde removal of the embolus was combined with milking of the iliac arteries. In 2 cases the operative approach was not stated. In summary, there were 10 successful cases

From the Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts.

reported in which a direct approach had been made on the bifurcation of the aorta by either a transperitoneal or retroperitoneal exposure, and 7 cases in which the embolus had been removed by retrograde methods. In the author's experience the indirect method of embolectomy by retrograde instrumentation has resulted in a much lower percentage of successful results because, first, it may be difficult to ascertain that all the thrombus has been removed, and, second, the intima frequently is traumatized which may result in secondary thrombosis, and, third, the instrumentation causes marked vasoconstriction with the narrowing of the arterial lumen due to reflex vasospasm, a condition that also favors secondary thrombosis. For these reasons a direct exposure of the site of embolism, whenever possible, is considered to be of extreme importance in obtaining a successful result. The majority of reported successful embolectomies have been for embolism at the bifurcation of the common femoral artery. This is true chiefly because the location of the femoral artery permits easy exposure so that the vessel can be isolated and visualized both proximal and distal to the site of embolism.

The third principle is that the main artery distal to the site of embolism should be temporarily occluded without traumatizing its wall before exposure of the artery at the site of embolism or proximal to it is attempted. If this is not done there is great danger that the embolus will be dislodged and driven more distalward in the arterial tree or that the embolus may be fragmented, resulting in multiple embolisms. In the case of a rider embolus at the bifurcation of the aorta, it is necessary first to isolate and occlude, with a nontraumatizing type of clamp, both the right and left common iliac arteries.

The fourth principle is that, after opening the artery, the intima should not be traumatized, since such injury may result in secondary thrombus formation with occlusion of the vessel after closure of the arteriotomy wound. For this reason it is preferable not to insert an instrument into the arterial lumen to extract the embolus. The arterial pressure from above will always force the embolus out especially if one gently manipulates the artery with the fingers at the site of the embolism (Fig. 2). If a secondary thrombus has formed distal to the embolus, it is best removed by milking it upward. If it has extended distalward for a considerable distance, suction with a small well lubricated catheter may be resorted to, but usually in such cases it is impossible to remove it completely to restore circulation.

The fifth principle is that complete control of the arterial inflow, both proximal and distal to the arteriotomy, is absolutely essential for the best results. If bleeding occurs during the suturing of it, great difficulty will be encountered because the flow of blood obscures the wound edges. In addition without hemostasis the blood in the segments of arteries isolated between clamps will be apt to clot during the closure. This may result in complete thrombosis at the site of embolectomy or the thrombus may be dislodged, when the arterial flow is released, to produce a secondary embolism.

The sixth principle is that the arteriotomy should be closed with meticulous care by a fine nonabsorbable type of suture that is attached to the end of the needle, the so called atraumatic suture. These are manufactured as arterial sutures and may be obtained from the surgical supply houses. The correct method of closing an arteriotomy incision is that the intima of one side should be approximated to the intima of the opposite side. A mattress suture going through all layers of the vessel wall is first placed at the middle of the arteriotomy wound. This produces eversion of the wound edges so that intima is approximated to intima. The closure is then completed by a continuous running over-and-over type of suture, commencing at the proximal end of the arteriotomy wound (Fig. 3). The suture should be pulled taut with each stitch, so that the suture material does not lie exposed in the arterial lumen. This type of closure will give complete hemostasis, so that it is unnecessary to utilize any reinforcing measures.

METHOD OF ARTERIAL CONTROL

A number of methods have been described for the temporary occlusion of the arteries proximal and distal to the site of embolism. Traction on a piece of flexible rubber tubing or braided cotton tape drawn around the

artery is the most common technique described in the literature: Allen, Danzis, Key, Lund, Murray, and others. The chief advantage of this method is that either of the materials is always available in any operating room. There are disadvantages, however, which outweigh this advantage. In the first place if direct traction is used, it is necessary to apply considerable force to occlude the arterial blood flow, since the pressure by the tubing or tape is applied only to the under surface of the artery. The vessel being an elastic structure tends to stretch so that it is necessary to angulate it to a considerable degree before the lumen is completely occluded (Fig. 4). This requires considerable force so that there is danger of fracturing the arterial wall. If the material is twisted at the same time traction is exerted (Key and Murray) less force is necessary. It is impossible to obtain complete control of the arterial flow, in either case, without the continual application of excessive force. The method is cumbersome and unwieldly since the usual embolectomy requires three points of temporary arterial occlusion, one proximal and two distal to the embolus, so at least three hands are necessary to effect control of the arterial flow. In the small operative field used for embolectomy the surgeon is handicapped for this reason for his assistants will not be able to help him to the greatest advantage.

The method described by Wikle and Cabot, in which they occluded the aorta by tying it temporarily with a cotton tape ligature, is open to criticism because of the danger of fracturing the wall of the aorta. The placing of a short piece of rubber tube over the artery and incorporating it in the temporary ligature, as recommended by Gage and Ochsner, is an improvement in this method, but the ligature may be drawn too tight and thus damage the vessel wall. Another disadvantage to the ligature method of temporary arterial control is that it is necessary to sever the ligatures after removal of the embolus when the collateral circulation is being tested and it is being ascertained if all the embolus has been removed, following which new temporary ligature must be applied in order to suture the arteriotomy wound.

The use of a Crile arterial clamp (Fig. 5) has not been found to be satisfactory, as it is difficult to apply and release. In addition it is dangerous since the clamp is tightened with a screw which allows an enormous mechanical advantage, so that irreparable damage may be done to the vessel. Pearse, Lesser, and Murray advocate the use of rubber shod "bulldog" arterial clamps (Fig. 5). The advantage of these is that they do not traumatize the arterial wall and they may be readily applied and released. The chief drawback to them is that they may be dislodged readily or even slip off by themselves due to the slipperiness of the rubber covering. Furthermore the jaws of the clamps may not be long enough to permit their use on the common iliac artery in doing an aortic embolectomy.

After these various methods were tried and their disadvantages were realized, a different type of arterial control was developed. The ideal method of occluding an artery is to flatten it, by opposing one side of its lumen against the opposite one (Fig. 4). In order to obtain this type of occlusion without danger of having the clamp slip off at a crucial moment, the Bethune lobectomy tourniquet (Fig. 6) has been utilized. This is a modification of Shenstone's tourniquet. It consists of a "T" shaped metal rod with notches on it into which fits a ratchet that may be moved up and down on the rod. There are two apertures in the short limb of the "T" through which a heavy braided cotton cord passes, forming a loop. The two ends of the cord are tied to the ratchet so that the loop may be made large or small as desired. The cord must be untied to apply the clamp to a vessel and an end unthreaded from the short limb of the "T" then drawn around the vessel, rethreaded in the instrument, and retied with a square knot to the ratchet. The vessel then may be occluded readily by closure of the loop which needs only one hand. Care must be taken not to close it too tightly, otherwise the vessel wall will be injured. It will be found that only the most gentle pressure is needed even to occlude as large a vessel as the aorta or common iliac artery. Once the clamp is in place, the vessel can be occluded or released readily at a moment's notice. This attribute is of the greatest value in the opera-

tion of embolectomy, since one has the feeling of complete complacency in being able to control the arterial blood flow once the embolus has been removed. In addition it permits the absolute control during the suturing of the arteriotomy wound. It is readily removed by cutting the cotton cord.

The use of this clamp has made it possible to devise a new and more simple type of embolectomy for a rider embolus at the bifurcation of the aorta (Fig. 1). The advantage of this method is that it is unnecessary to dissect the aorta free in order to control the arterial blood flow. This eliminates the danger of injury to this large vessel which might be catastrophic. The anesthesia of choice in good risk patients is spinal, since this gives such complete relaxation of the abdominal muscles. In the poor risk patient ether anesthesia, administered through an endotracheal tube, is preferable.

TECHNIQUE OF AORTIC EMBOLECTOMY

The bifurcation of the aorta may be exposed either transperitoneally or extraperitoneally through a right paramedian abdominal incision, and the rectus muscle retracted lateralward. Murray has recommended the extraperitoneal approach, but in the case reported the transperitoneal method was used. The chief advantage of the latter is that it gives a more direct approach with less retroperitoneal dissection. The extraperitoneal exposure is preferable in obese patients because retraction of the intestines and exposure of the large arteries is more readily obtained. The incision should commence about 2 inches above the umbilicus and extend down to the pubis. If the transperitoneal approach is used the intestines are carefully displaced upward and held with large moist gauze packs. The common iliac arteries and the bifurcation of the aorta are exposed by incising the peritoneum in a triangular fashion over these vessels so that a flap of it can be turned downward. The right ureter should be visualized to avoid damage to it, but it is unnecessary to isolate it. The next step is carefully to free up the right common iliac artery just proximal to its bifurcation. A Bethune clamp is applied at this point and the artery is immediately occluded. Then the left common iliac artery is isolated. A second tourniquet is applied and the artery occluded just distal to the portion of the embolus which extends into its lumen. With both the right and the left common iliac arteries occluded in this manner the embolus is trapped so that if dislodged there is no danger that it will escape to lodge more distal in the arterial tree (Fig. 1).

The next step is to apply a third tourniquet around the proximal end of the right common iliac artery as near the aortic bifurcation as possible. This clamp is left open but arranged so that it can be closed immediately after removal of the embolus. After the iliac arteries have been controlled in this manner the adventitia is carefully dissected from the mid portion of the anterior surface of the right common iliac artery. A 1.0 to 1.5 centimeter longitudinal incision is made through the vessel wall in this area. The length of it should be no greater than the diameter of the artery. The bifurcation of the aorta is then gently manipulated with the fingers to dislodge the embolus (Fig. 2). Since the left common iliac artery has been occluded just distal to the embolus the arterial pressure forces it into the right common iliac artery. The embolus is rapidly extruded by the tremendous force of the blood. It is not necessary to extract the thrombus by instrumentation within the arterial lumen. If it becomes stuck in the arteriotomy wound, gentle squeezing of the artery from above down will aid in its extrusion. A tremendous gush of blood follows the embolus, which is immediately controlled by closing the tourniquet proximal to the arteriotomy wound. This hemorrhage may be terrifying even for the experienced surgeon if preliminary adequate control of the artery has not been obtained. With a rubber tubing around the artery extreme force may be necessary to control it, and danger of damaging the arterial wall by an overzealous assistant is real. The greatest value of the Bethune tourniquet in embolectomy is in this step of the operation, since by the gentlest of pressure the arterial flow may be completely stopped. The surgeon is able with one hand to dislodge the embolus while with the other on the clamp he can instantaneously close it after extrusion

Fig. 1. A drawing to show the technique of a transperitoneal aortic embolectomy through a right paramedian incision. The bifurcation of the aorta and the common iliac arteries are exposed by incising and reflecting downward the posterior peritoneum. The method of applying the tourniquet clamps (Bethune type) is shown. They are applied in the following order: the first one is placed on the right common iliac artery just proximal to its bifurcation; the second one on the left common iliac artery at the distal end of the embolus; and the third one on the right common iliac artery at its origin. The first two clamps are closed while the third remains open until the embolus has been extruded, then it is closed. The arteriotomy is between the two clamps on the right common iliac artery.

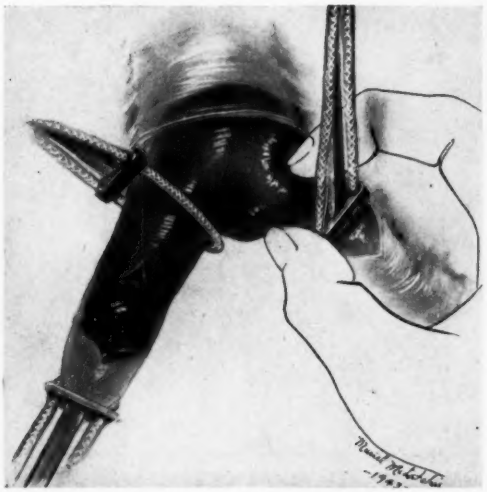


Fig. 2. The method of digital mobilization of the embolus and its extrusion through the arteriotomy in the right common iliac artery.

of the embolus. He therefore has the situation under control at all times.

After the main thrombus has been extruded the left common iliac artery and the bifurcation of the aorta should be carefully palpated for additional clots. The proximal clamp on the right common iliac artery should be released to allow blood to escape and carry with it any clot remnants to make certain none remain. The clamp is again closed after it is ascertained that there is an active pulsating flow of arterial blood. Every effort should be made to obtain this; otherwise it is certain that occluding thrombi are still present. Then the distal clamp on the same artery is opened with the proximal one closed. Free bleeding should result, indicating that the collateral channels and the bifurcation of the common iliac artery are free of thrombi. If active arterial bleeding does not occur, exploration should be carried out to remove any fragments of the original embolus lodged in this location. The patency of the left common iliac artery should be tested by releasing the tourniquet on it. If pulsations are demonstrable in the external iliac artery this is sufficient evidence that the left common iliac is patent. If not present it means that another embolus is occluding the bifurcation of the latter, and an embolectomy must be performed at this site to restore the circulation of the left lower extremity. These secondary emboli rarely occur, but they should be looked for and removed if present. When it is ascertained that there is free bleeding from above and below, the arteriotomy incision is closed.

Fig. 3. The intima-to-intima closure of the arteriotomy is shown with a centrally placed single everting type of mattress suture and a continuous hemostatic suture of fine silk.

At this stage in the operation, the use of the tourniquet is advantageous in that complete control of the vessels proximal and distal to the incision is obtained, so that the edges of the wound are not obscured by escaping blood. Hemostasis is also so effective that little if any blood will be trapped to form a secondary thrombus in the occluded segment of the right common iliac artery during the closure of the arteriotomy wound. As a safeguard in case a small amount of blood may be present, 500 units of heparin in a few cubic centimeters of normal saline are placed in the vessel lumen, as has also been recommended by Murray. The incision is closed as previously described with a fine nonabsorbable suture. The placing of a mattress suture through all layers of the vessel wall is a useful step to evert the wound edges and permit intima-to-intima closure with a continuous suture.

The tourniquets are removed after the incision is closed. The order in which this should be done is, first, the distal tourniquet on the right iliac artery, then the one on the left iliac artery, and last the proximal one on the right iliac artery. The incision in the posterior peritoneum is closed carefully with a running suture of No. 0000 chromic catgut. The abdominal wound is closed in layers without drainage. Heparin is administered by a continuous intravenous drip for 24 hours following embolectomy, if the circulation has been restored, as evidenced by a return of pulsations in the peripheral arteries. This is an additional safeguard against secondary thrombosis at the arteriotomy incision. If the circulation has not been restored completely, the heparin should be continued for a longer period. A clotting time of 20 to 30 minutes should be maintained during the period of heparinization.

CASE REPORT

M. E. S., No. 77,845, a white single female stenographer, aged 39 years was admitted to the Baker Memorial division of the Massachusetts General Hospital October 19, 1942, for treatment of pneumonia of 1 week's duration. This was her 4th hospital admission. The first 2 were at the Massachusetts Eye and Ear Infirmary for treatment of toxic amblyopia in September and October, 1937. The 3rd admission was on December 26, 1940, for the

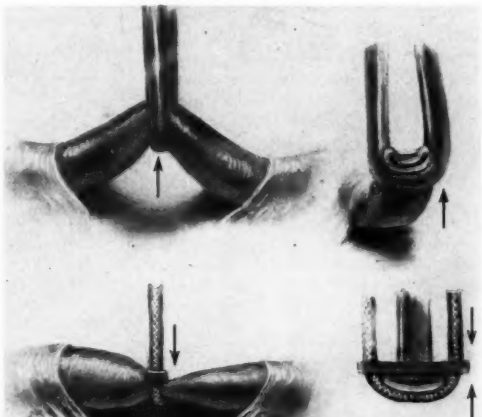


Fig. 4. Drawings to compare arterial occlusion by means of traction on a rubber tube (upper two) and by a tourniquet clamp (lower two). The arrows indicate the direction of the force applied. Note the angulating of the vessel necessary for occlusion with the tubing, indicating the application of considerable force; whereas closure with the clamp requires a relatively small force without disturbing the artery.

a b

Fig. 5. a, Drawing of a Crile arterial clamp. The screw control permits too great a mechanical advantage so the force applied to the arterial wall may damage it. b, Drawing of a "bull-dog" clamp. The disadvantage of it is that it tends to slip off the artery.

Fig. 6. Drawing of a Bethune type of tourniquet clamp. Its advantages are ease of application, readiness of closure, and the small amount of force necessary to occlude an artery, preventing damage of its walls.

treatment of bronchopneumonia, rheumatic heart disease with mitral stenosis and auricular fibrillation. She was discharged improved on January 11, 1941.

At the age of 1 year she had had inflammatory rheumatism, at 16 years a streptococcus infection of the throat, and at 18 chorea. A diagnosis of inactive rheumatic heart disease with mitral stenosis and insufficiency with cardiac hypertrophy was made in October, 1937. There was no evidence of cardiac failure. The remainder of her past history is irrelevant.

Physical examination showed a moderately well developed and nourished woman lying in bed. The general physical examination was negative, except for her lungs and heart. Over the right lower lung field posteriorly there were noted decreased resonance, diminished breath sounds, and increased tactile fremitus and some loud râles. The remainder of the lung fields was clear. Examination of the heart showed a regular rate of 120 per minute. The first sound at the apex was marked by a systolic murmur and a low pitched late diastolic murmur with crescendo. There was apical diastolic thrill; a systolic murmur was heard at the 3rd left interspace without a thrill. The blood pressure was 110/80. A diagnosis of inactive rheumatic heart disease with mitral stenosis and insufficiency, cardiac hypertrophy, and pneumonia in the right posterior lobe was made. The white blood count was 15,100, 86 per cent polymorphonuclear leucocytes. The urine had a specific gravity of 1.017, and was negative for albumin and sugar. The patient's temperature was 101 degrees Fahrenheit.

After admission the patient was placed on oral sulfadiazine treatment. She made a satisfactory response to this and was making a normal convalescence until 10:30 p.m. on October 25. At this time while the patient was walking to her bed from the bathroom she suddenly felt numbness in both feet. In bed she noticed that her heart began to pound, the numbness became more marked and extended upward and became very uncomfortable with tingling in her legs. At this time her heart rate was 112, grossly irregular. Examination of her feet showed they were cold and there were no arterial pulsations felt in either leg including the femoral arteries in the groins. A diagnosis of a rider embolus at the bifurcation of the aorta was made. The absence of pulsations in her legs was confirmed by oscillometry which showed no oscillations in either extremity.

At 1:30 a.m., October 26, 3 hours after the time of embolism, an operation was performed according to the technique described, and an embolus obstructing the bifurcation of the aorta was removed (Fig. 7). Spinal anesthesia was employed, 16 milligrams of pontocaine crystals being used. Following the re-

Fig. 7. The embolus removed from the bifurcation of the aorta in the case that is presented.

moval of the embolus there was an immediate return of the arterial circulation as evidenced by pulsations in both feet. Intravenous heparin was given for 24 hours following the operation, and the coagulation time of the blood was maintained at 25 minutes.

Following the operation the patient made a very uneventful convalescence and was discharged from the hospital November 10, 16 days after the embolectomy. A follow-up on the patient 16 months after the operation still showed excellent circulation in her legs with pulsations in the right and left dorsalis pedis and posterior tibial arteries.

CONCLUSIONS

The success of an embolectomy depends on: (1) early operation, (2) direct and adequate exposure of the site of embolism, (3) occlusion of the artery distal to the embolus before the artery is disturbed at or proximal to the site of embolism, (4) avoidance of damage to the intima, (5) complete control of the arterial inflow both proximal and distal to the arteriotomy so that (6) a meticulous intima-to-intima closure may be accomplished.

The removal of a saddle embolus at the bifurcation of the aorta is a feasible operation if these principles are followed.

The technique of the operation has been simplified by the use of the tourniquet type of clamp for control of the arteries during the embolectomy.

A saddle embolus at the bifurcation of the aorta may be removed readily through an arteriotomy of the right common iliac artery, with two clamps on this blood vessel and one on the left common iliac artery, without the necessity of freeing up the aorta.

Embolectomy is more readily accomplished by direct exposure of the site of embolism. For this reason a transperitoneal or extraperitoneal approach through a right paramedian incision is recommended for the exposure of the bifurcation of the aorta and the common iliac arteries.

REFERENCES

1. Allen, A. W. N. England J. M., 1929, 201: 304.
2. Bauer, F. Zbl. Chir., 1913, 40: 1945.
3. Bethune, N. Canad. M. Ass. J., 1936, 35: 656.
4. Danzis, M. Ann. Surg., 1933, 98: 249.
5. Gage, M., and Ochsner, A. Ann. Surg., 1940, 112: 938.
6. Key, E. Brit. J. Surg., 1936, 24: 350.
7. Lesser, A. J. Am. M. Ass., 1943, 122: 285.
8. Linton, R. R. N. England J. M., 1941, 224: 189.
9. Lund, C. C. Ann. Surg., 1937, 106: 880.
10. McClure, R. D., and Harkins, H. N. Surgery, 1943, 14: 747.
11. Murray, G. Surg. Gyn. Obst., 1943, 77: 157.
12. Pearse, Jr., H. E. Ann. Surg., 1933, 98:17.
13. Ravdin, I. S., and Wood, F.C. Ann. Surg., 1941, 114: 834.
14. Shenstone, N. S., and James, R. M. Canad. M. Ass. J., 1932, 27: 138.
15. Wikle, H. T., and Cabot, N. Surgery, 1943, 13:264.

FURTHER STUDIES ON THE DIAGNOSIS OF BONE TUMORS BY ASPIRATION BIOPSY

RUTH EVELYN SNYDER, M.D., and BRADLEY L. COLEY, M.D., F.A.C.S., Colonel M.C., A.U.S., New York, New York

THE first report from Memorial Hospital on the diagnosis of bone tumors by aspiration biopsy was made in 1931 by Coley, Sharp, and Ellis. Their study was based on 35 cases at a time when this method was in an experimental stage. In all but 1 case tissue was obtained and the operative diagnosis in all but 2 cases proved correct. Three years later (1934) Martin and Ellis (4) made a more exhaustive study of the use of aspiration biopsy, at which time 1400 tumors of all types including 140 bone lesions had been aspirated. Coley (2) in the same year in a discussion of Bloodgood's paper on biopsy of bone tabulated 100 cases of bone aspirations, in 75 of which the diagnosis had been established. In the remaining 25 there were 3 false positives, i.e., a diagnosis of malignant tumor was made but there were errors in the type of cell reported; in 22 either no tissue or insufficient material for diagnosis was obtained.

Aspiration biopsy of tumors of bone has now become an established routine in the Bone Tumor Department of Memorial Hospital, and we feel therefore that a more recent analysis of results of this procedure is justified. This study includes 567 aspirations of 474 individuals done in the last 12 years in which charts and reasonable follow-up are available. The head and jaw regions are not included. Repeat aspirations were necessary for various reasons: failure of the first aspiration, confirmation of the first aspiration or for additional information, multiple or recurrent involvement of bones, or as a follow-up on treatment.

In this series it should be borne in mind that not all patients with bone lesions seen at Memorial Hospital have had aspiration biopsy; hence the figures given represent only a fraction of all the cases seen in the Bone Tumor Department. Many enter with the diagnosis already established at other institutions. Others in which it is felt that aspiration cannot yield diagnostic material or in which surgery is elected as the method of treatment are immediately subjected to operation. Tumors of the head and jaw region are not included, although several of these cases had the diagnosis established by aspiration of the skull. The aspirations have been done by many different operators, some of them inexperienced, so that failure to obtain tissue may have been the fault of the individual and not of the method. Practically every bone of the trunk and extremities has been the site of aspiration as shown by the following tabulation: femur, 146; pelvis, 111; ribs, 72; humerus, 52; scapula, 37; tibia, 40; sternum and clavicle, 33; vertebrae, 24; fibula, 21; small bones, 12; radius, 11; ulna, 8.

Cases have been classified according to the clinician's final diagnosis, based on clinical course, x-ray examination, operation, aspiration biopsy and in some cases autopsy findings. Where there was doubt as to the exact type of tumor the case was placed in a separate miscellaneous group. A number of bone lesions not considered bone tumors are seen at Memorial Hospital and must be differentiated from tumor. Some of these are suitable for aspiration though tissue obtained is frequently not satisfactory for diagnosis. It is in the field of true neoplasms that aspiration proves most valuable.

The advantages of aspiration biopsy have been frequently emphasized and will be reviewed here only briefly. It is a simple, rapid, economical procedure. It may clear up a questionable diagnosis or provide histological material in an obvious case without the need for hospitalization and preliminary operation. In many instances it provides microscopic proof for inoperable cases. While an open biopsy

From the Bone Tumor Department, Memorial Hospital, New York.

TABLE I.—ASPIRATION BIOPSY OF BONE LESIONS

Diagnosis	Total cases	Aspiration diagnostic	Tissue obtained but not specific	Satisfactory aspirations	Malignant called benign	Benign called malignant	Aspiration insufficient	Repeat aspirations
Osteogenic sarcoma (all histologic types)	132	67	34	101	2	0	29	27
Endothelial myeloma (Ewing's)	42	29	9	38	0	0	5	6
Myeloma (plasma cell and other)	38	26	3	29	2	0	7	9
Giant cell tumor	30	25	3	28	0	0	2	4
Reticulum cell sarcoma	4	3	1	4	0	0	0	1
Liposarcoma	1	0	1	1	0	0	0	0
Angiosarcoma	3	0	2	2	0	0	1	1
Metastatic carcinoma	107	88	6	94	0	0	13	25
Miscellaneous malignant tumors	16	8	4	12	1	0	7	3
Hodgkin's disease	3	0	1	1	0	0	2	1
Miscellaneous benign tumors (chondroma, chondromatous giant cell, hemangioma)	18	9	1	10	0	1	7	3
Bone cysts	7	0	4	4	0	0	3	0
Paget's disease	6	1	0	1	0	0	5	0
Lipoid histiocytosis	4	2	1	3	0	0	1	2
Inflammatory disease	45	7	16	23	0	0	22	9
Miscellaneous unclassified benign	18	0	0	0	0	0	18	0
Total	474	269	91	360	5	1	119	93
Repeat	93							
Total aspirations	567							

may eventually be necessary, no time is lost by aspirating first and it frequently eliminates the more formidable procedure with its attendant hazards of nonhealing and other operative complications.

The foremost disadvantage of this method of diagnosis is the difficulty of interpretation. The pathologist is called upon to make a diagnosis from a minute bit of tissue or from isolated cells and this requires unusual skill and experience. The late Dr. James Ewing, Dr. Fred Stewart, and Dr. Frank Foote of the department of pathology have made careful studies of all material submitted, and it is largely because of their co-operation and skillful interpretation that the value of this method of diagnosis has become established. Stewart emphasizes that the clinical setting, the site of aspiration, the normal cells of this region, and the possible tumors occurring in this location all must be known in order to be able to recognize and interpret the abnormal cells. It is not the aim of the pathologist to classify the tumor precisely in every case, but rather to state whether or not it is malignant and whether or not it is a primary or metastatic tumor. In the present series we have regarded the aspiration as successful if a diagnosis of malignant tumor has been returned. However in many instances, especially when a clot for section has been obtained, exact type diagnosis has been made. In inflammatory diseases if pus was obtained and other findings are consistent with a benign process the aspiration was also considered satisfactory.

It may be argued that the aspiration may implant tumor cells in the path of the needle, that it may produce hemorrhage in the tumor, or loosen cells into the blood stream, thus producing metastases. In no case have we noted any immediate untoward effects. We have not seen development of tumor at or about the site of the needle puncture which would indicate that implantation of tumor cells had occurred along the tract nor has there been any evidence that metastasis was produced or has-

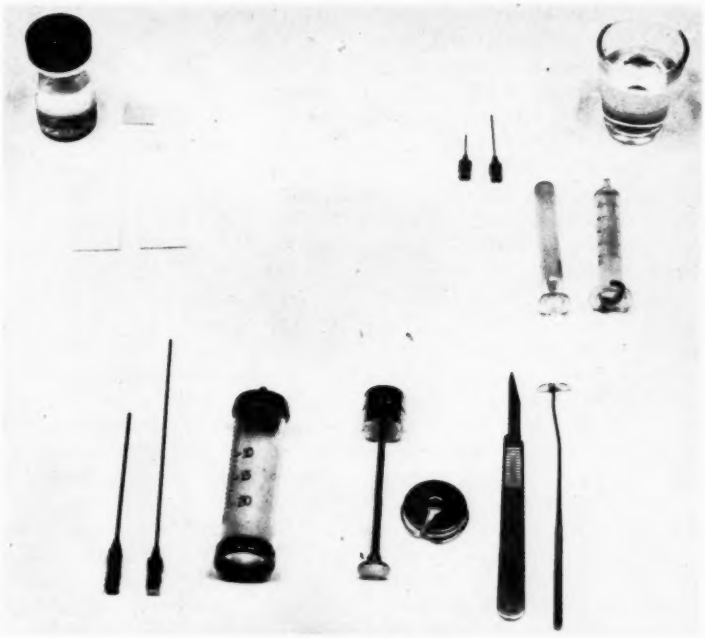


Fig. 1. Aspiration biopsy set.

tened by the aspiration in any case in which distant disease later developed. In support of this we cite the results of a study of the cases of osteogenic sarcoma seen during the 5 year period from 1932 through 1936. Of a total of 118 cases, 62 were aspirated and 56 were not. Nine of those aspirated have survived for 5 years or more without evidence of disease (survival rate of 14.5 per cent). Eight of those not aspirated survived for 5 years or more (survival rate of 14.3 per cent). In this series at least it would seem that there is no evidence that aspiration had been a detriment to survival in a disease which at best has a poor prognosis.

TECHNIQUE

Since the method of obtaining and preparing the material has been fully described by Martin and Ellis (5), we will review it only briefly. Occasionally in infants, young children or highly apprehensive adults, a short gas anesthesia or intravenous sodium pentothal is used. Fluoroscopic guidance is sometimes necessary when the lesion is poorly accessible or when it is in the neighborhood of important anatomical structures. Blady has described the technique for aspiration biopsy in difficult locations. The approach is determined by the roentgenographic appearance. The site should be carefully chosen and usually should be at a point where there is a break in the continuity of the cortex or where there is extension of the tumor into soft tissues. Failure to obtain cells occurs most frequently in sclerosing or intramedullary lesions.

The instruments needed are illustrated in Figure 1. A 20 cubic centimeter record syringe tightly fitted with an 18 gauge needle from 5 to 12 centimeters long is used. The skin is prepared with iodine and alcohol and a small area infiltrated with 1 per cent novocain. A stab wound is made through the skin with a bistoury-pointed scalpel (No. 11 Bard Parker blade). The needle is inserted and advanced slowly to the site of the lesion; it can be felt to enter tumor tissue when there is soft tissue extension. In other cases increased pressure must be exerted to puncture the cortex of the

bone. A vacuum is then produced by partially withdrawing the piston and the needle is advanced into the tumor for about a centimeter or the needle is given a rotary motion while maintaining the suction. This manipulation is repeated a number of times, the vacuum being renewed frequently. The piston is then slowly released and the syringe and needle withdrawn. The vacuum must be released before removal or the contents of the needle will be sucked into the syringe, making collection difficult. Usually the needle will be found to contain a plug of blood and tissue which can be carefully forced out or pushed out with an obturator. The barrel of the syringe is also carefully examined and bits of tissue and blood clot are removed. A portion of the material is placed on a slide and a second slide is placed over it. Using firm pressure the tissue is crushed thin and drawn across lengthwise. These slides are immediately stained and examined. The remaining tissue and blood are massed together on a small square of blotting paper and dropped into a specimen bottle containing 10 per cent formalin and run through as paraffin sections.

The slides are stained and ready for diagnosis in from 6 to 8 minutes. Each slide is fixed by heating gently over a gas flame. It is then stained as follows, the time being a flexible element depending on the progress of the staining: (1) alcohol 95 per cent, 1 minute; (2) water, 1 minute; (3) hematoxylin, 1 minute; (4) water, 1 minute. (5) Check cellular stain microscopically and if insufficient, return to hematoxylin for deeper staining; (6) eosin, 1 minute, check microscopically; (7) alcohol, 95 per cent, ½ minute; (8) carbol-xylol, ½ minute; (9) xylol, ½ minute. (10) Mount with Canada balsam and cover glass.

The clot is treated as a small biopsy, care being taken to preserve every particle of tissue. It is carried through the stages of alcohol fixation and embedding in paraffin. Fresh 52 to 56 degrees C. paraffin should be used for embedding and all particles massed together on the block and cooled immediately on ice. Sections from different levels of the block are cut. For a more rapid technique requiring about 3 hours for preparation the following method is used: (1) formalin 10 per cent, 10 minutes; (2) alcohol 95 per cent, two changes, 10 minutes each; (3) xylol, two changes, ½ hour each; (4) paraffin 56 degrees C., two changes, ½ hour each—(first three steps in incubator at 37 degrees C.); (5) cut and stain.

Osteogenic sarcoma. Osteogenic sarcoma comprises our largest group submitted to aspiration biopsy, 132 cases being included. Under this classification we include all types of osteogenic and chondrosarcoma. Of these, 67 or 53 per cent were classified as osteogenic sarcoma on smear or sectioned clot while an additional 34 were called malignant tumor, type not determined. Thus in 76 per cent a definite diagnosis of malignant tumor was made without resorting to a formal biopsy. Two were reported as benign tumors. One of these was a lesion of the ilium which was reported as "chondroma in this section but does not exclude sarcoma in other parts," and the patient subsequently died of pulmonary metastasis. The other was an unusual case of low grade osteogenic sarcoma of the proximal phalanx of the fifth finger which was reported as "consistent with giant cell tumor." This patient, incidentally, is living and well without evidence of disease 7 years after operation. In only 29 cases (22 per cent) did aspiration fail to yield tissue or yielded insufficient tissue for interpretation.

Endothelial myeloma (*Ewing's sarcoma*). Of a total of 42 cases, 31 had positive aspirations and an additional 6 were diagnosed as malignant tumor unable to classify or unable to differentiate from osteogenic sarcoma. This is significant in view of the fact that endothelioma and osteogenic sarcoma are often difficult or impossible to differentiate on the basis of the roentgenographic appearance. Only 5 failed to yield diagnostic material, making a positive percentage of 89. It is of interest to note that 2 of these cases had had previous open biopsies early in their course which showed only chronic osteitis in the tissue obtained. Both died shortly of multiple lesions. In each of these cases small doses of x-ray had been administered prior to the biopsy. This is contrary to our practice. We believe that the diagnosis should be established before any treatment is begun as even a single exposure to roentgen-rays may mask a tissue diagnosis

of endothelioma with false reassurance and tragic outcome.

Myeloma. Under this classification are included plasma cell myeloma and other far rarer types of myeloma. Aspiration biopsy was carried out in 38 cases of which 27 (71 per cent) were diagnosed definitely or probably as myeloma. One case on two occasions was reported questionably as metastatic carcinoma; at autopsy, however, it proved to be an erythroblastic myeloma of Warren's type. In 2 instances a diagnosis of benign tumor was made. One of these was a previously irradiated case called giant cell tumor on smear; the other was called myxoma but the patient died with the usual course of myeloma. In one case a differential between metastasis and myeloma could not be made. In the remaining 7 cases no cells were obtained. In several instances the difficult differential diagnosis of myeloma or metastatic carcinoma was made.

Giant cell tumor. Of 34 giant cell tumors of bone aspirated, 26 or 76 per cent were diagnosed as giant cell tumor. One of these was regarded as malignant and proved to be so at operation. Two others showed malignant recurrence but aspirations were not diagnostic. In several cases the course of the disease during treatment has been followed. Aspiration biopsy of giant cell tumor may not be successful because of a dense surrounding cortex which may act as a barrier to the needle.

Reticulum cell sarcoma of bone. The clot obtained by aspiration in 3 cases was diagnosed by Dr. Stewart as primary reticulum cell sarcoma. A fourth was called malignant tumor and proved to be reticulum cell sarcoma at operation.

Liposarcoma. One case has been classified as liposarcoma on the basis of open biopsy which was called spindle cell sarcoma at aspiration. An exact cell type diagnosis could not be expected from an aspiration biopsy.

Angiosarcoma. Three cases classified as angiosarcoma have been included in this study. Tissue was obtained in 2 instances and interpreted as endothelioma but the resected specimens showed angiosarcoma.

Miscellaneous malignant tumors. We have placed in this group 16 miscellaneous type tumors, some of them unclassified. Six of 7 chordomas and 1 ganglionic glioma were positive. Two cases of polyostotic fibrous dysplasia with sarcoma in one bone showed malignant tumor at aspiration, one of which was called osteogenic sarcoma. Four cases showed malignant tumor, but no classification was made either by biopsy or clinically. The remaining two aspirations were not successful and the type of malignant tumor was never proved.

Metastatic carcinoma. Our second largest group aspirated was metastatic carcinoma, a total of 107 cases being tabulated. During the course of a year many metastatic lesions of bone are encountered. In the majority the primary is probably known. Aspiration biopsy is not a routine when the metastasis is obvious but there are frequent instances of bone involvement with no definite indication of a primary lesion. Here a differential diagnosis must be made between metastatic carcinoma and primary bone tumor or occasionally from an inflammatory lesion. In most cases there is involvement of ribs, vertebrae, or pelvic bones. Any surgical procedure can be justified only for diagnosis and aspiration biopsy has therefore proved itself to be of distinct value. Of the 107 cases aspirated, the biopsy was positive for metastasis in 90 or 84 per cent. In 4 additional cases "malignant tumor unclassified" was reported, making 88 per cent satisfactory for a diagnosis of malignant tumor. In 25 instances the pathologist was able to recognize the organ from which the metastasis originated while in 24 others he was able to identify the type of cell (adenocarcinoma, epidermoid, etc.).

Hodgkin's disease. Formal sections are considered necessary for a diagnosis in disease of this type when it occurs in soft parts or in bone. Aspiration is not usually done but 3 cases were aspirated, one of which showed caseous granuloma.

Benign tumors of bone. Most benign tumors are not suitable for aspiration biopsy and are not usually aspirated unless the roentgenographic picture is confusing. The material is frequently difficult to obtain and gives little information. Eighteen cases of chondroma, osteochondroma, chondromatous giant cell variant and hemangioma were aspirated. Eight

of these were positive. One case was called chondrosarcoma of the distal end of the fibula but its roentgen appearance was that of a benign tumor and local resection showed chondromyxoma only. This is the only instance of a definite false positive, i.e. where a benign tumor was called malignant. This is highly significant and important for it means that a report of a malignant tumor can be relied upon at this hospital. It is also well recognized by the clinicians that failure to obtain tissue or material that is diagnostic does not mean that the lesion is not malignant unless all other factors are taken into consideration.

Bone cysts. Cysts are unsatisfactory for aspiration, and this procedure is usually not carried out. Seven cysts were aspirated without positive findings except that fluid was obtained in a few instances.

Osteitis deformans. This group is also not satisfactory for aspiration and the procedure is not recommended. One of 6 cases of Paget's disease aspirated yielded material consistent with this diagnosis.

Lipoid histiocytosis. Diseases of this type are occasionally seen and must be differentiated from tumor. One case of Hand-Schuller-Christian's disease and one of Nieman-Pick's with bone changes had the diagnosis established by aspiration. One case of eosinophilic granuloma was called questionably as myeloma and a second case was not diagnostic.

Inflammatory disease of bone. Forty-five patients with inflammatory disease of bone were aspirated, the diagnosis being based on a negative aspiration plus an open biopsy in some cases, the roentgenographic appearance, clinical course, and history. In 16 cases pus or granulations was obtained and in 7 of 8 cases of tuberculosis the diagnosis was proved by aspiration. The aspiration was of value from a "negative" standpoint. In none of these was a false positive reported.

Miscellaneous benign lesions of bone. There remain 18 cases in which no definite diagnosis was ever established or the condition classified but which were considered benign from their clinical course and other data. No tissue was obtained in any of these.

CONCLUSIONS

The results of 567 aspiration biopsies of bone on 474 individuals have been studied and reported, and are summarized in the table. There have been no immediate complications of the procedure and no evidence to suggest more rapid development of metastasis by the use of aspiration to establish diagnosis. In primary bone tumors and metastatic carcinoma of bone 385 cases have been aspirated, of which 67.5 per cent were definitely and specifically diagnostic while a total of 82 per cent showed material sufficient for the diagnosis of tumor, the exact type diagnosis not being called in 14.5 per cent. In only one instance was a diagnosis of malignant tumor made when the resected specimen showed a benign tumor and in this case the treatment was local resection. Thus in no case did a false aspiration diagnosis lead to amputation for a benign process. The clinician must understand the scope and limitations of the method and realize that failure to obtain cells means only that no tissue was obtained, further interpretation depending on the clinical and roentgenographic findings. At Memorial Hospital aspiration biopsy has proved itself to be a valuable and reliable diagnostic procedure.

REFERENCES

1. Blady, J. V. Am. J. Roentg., 1939, 42: 515–523.
2. Bloodgood, J. C. Am. J. Surg., 1934, 24: 331–344.
3. Coley, B. L., Sharp, G. S., and Ellis, E. B. Am. J. Surg., 1931, 13: 215–224.
4. Martin, H. E., and Ellis, E. B. Surg. Gyn. Obst., 1934, 59: 578–589.
5. Idem. Ann. Surg., 1930, 92: 169–181.
6. Stewart, F. W. Am. J. Path., 1933, 9: 801–812.

INTRAVENOUS ALCOHOL IN THE SURGICAL PATIENT

A Preliminary Report

DANIEL C. MOORE, M.D, and MARY KARP, M.D., Chicago, Illinois

ALCOHOL in its various forms has been a part of the medical profession's armamentarium since medieval times. Its use as a stimulant, analgesic, and anesthetic is well known. In 1929 Marin wrote his doctorial thesis on the subject of "Intravenous Anesthesia with Ethyl Alcohol" (1). The popularity of this method, however, was curtailed because its users reported such complications as hemolysis, sclerosis of the blood vessels, shock, and decreased urinary output. In 1939 Mueller reviewed a series of 2,000 cases in which 5 per cent and 10 per cent alcohol solutions were infused. Since this paper, a new interest has developed in intravenous alcohol from the analgesic and caloric standpoint. Dr. Vincent O'Conor has utilized 5 per cent alcohol for his operative cases since June of 1941. His excellent results with this method have stimulated our interests and have led us to expand its use to other surgical specialties. This report is based on an analysis of the last 150 cases.

The physiological effects of alcohol have been thoroughly investigated by many scientific workers (5, 8). When 1000 cubic centimeters to 3000 cubic centimeters of 5 per cent or 10 per cent alcohol in 5 per cent glucose is administered intravenously over a 24 hour period, the patient experiences a dulling of memory and concentration. He has a sense of well being and loss of anxiety. Respirations are increased (6), the blood pressure shows no significant change, the pulse may increase slightly, there is a vasodilatation, but the body temperature remains the same or decreases slightly. Alcohol does not have any bronchoconstrictor action and seldom any bronchodilator action as shown from determination of the dead space of breathing (6). Nausea and vomiting, acidosis, and headache are not concomitant symptoms when the alcohol is used intravenously; they do occur, however, when it is taken orally in comparable doses (3, 10, 12). There is an increase in the flow of urine which is due to the fluid intake, not to the diuretic effect of the alcohol alone. Ninety to ninety-nine per cent of the alcohol is completely oxidized in the body. Approximately 2 per cent is excreted in the urine, and from 0.2 per cent to 0.5 per cent is eliminated by the lungs. In our series of cases blood analyses have shown 0.2 milligram to 1.0 milligram alcohol per cubic centimeter of blood immediately after and during the course of administration. If the blood concentration of alcohol is above 0.5 to 0.7 milligram, the patient shows signs of inebriation (5, 9). The amount in the blood varies with the rate of infusion, metabolic rate, and tolerance of the patient (7). The official U. S. Navy test has been used in our determinations. The details of the test are as follows:

HEISE TEST

1. Take 2 c.c. of whole blood, plasma, or serum.
2. Add 15 c.c. of picric-tartrate reagent. Picric-tartrate reagent—one half saturated picric acid containing about 10% tartaric acid.
3. Distill and collect the first 10 c.c. of distillate.
4. Take 3 clean test tubes.
5. Add 1 c.c. of distillate to tube No. 1.
6. Add ½ c.c. of distillate plus ½ c.c. of distilled water to tube No. 2.
7. Add ¼ c.c. of distillate plus ¾ c.c. of distilled water to tube No. 3.
8. Add 1 c.c. of N/15 $K_2Cr_2O_7$ in 50 per cent H_2SO_4.
9. Place in a boiling water bath for 10 minutes.
10. Compare color of each tube with those of the standard, using the colorimeter.

The normal individual metabolizes approximately 10 cubic centimeters of pure alcohol per hour (8, 11). This rate is a constant one regardless of the concentration in the blood. If this level is exceeded, intoxication may occur. This basic fact must be kept in mind when the drug is administered. A 5 per cent alcoholic solution, there fore, will contain 10 cubic centimeters of 95 per cent alcohol per 200 cubic centimeters of fluid. In 1 hour this amount will be entirely metabolized in the average individual. Cautious additional amounts above this figure will give the milder forms of euphoria and intoxication which are needed for clinical results, as these vary with the individual tolerance. Therefore, it is best to judge the rate of infusion by the subjective signs.

The clinical uses of intravenous alcohol are mirrored through its many physiological effects. It has a special value in those cases in which nausea, vomiting, and paralytic ileus prevail (2, 3, 10, 12).

From the Department of Surgery, Northwestern University, Medical School and The Anesthesia Service, Wesley Memorial Hospital.

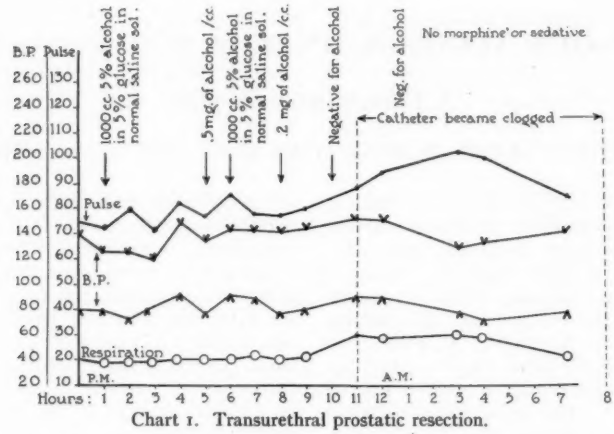

B.P. Pulse
1000 cc. 5% alcohol in 5% glucose in normal saline sol.
.5 mg. of alcohol /cc
1000 cc. 5% alcohol in 5% glucose in normal saline sol.
.2 mg of alcohol /cc.
Negative for alcohol
Neg. for alcohol
No morphine or sedative
Catheter became clogged
Pulse
B.P.
Respiration
P.M.
A.M.
Hours: 1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5 6 7 8

Chart 1. Transurethral prostatic resection.

These patients are starving. It is a known fact that a person in a normal state of health can support himself from his own body surpluses for 3 to 4 days without serious damage to his protein, carbohydrate, and fat stores. However, beyond this limit, the body starts to draw from its reserves. One thousand cubic centimeters of 5 per cent glucose in normal saline will provide 200 calories. With the addition of 50 cubic centimeters of 95 per cent alcohol, the caloric intake is increased to approximately 600 calories (3, 12). Thus, a solution of 5 per cent alcohol and 5 per cent glucose in physiological saline tends to protect the body proteins, carbohydrates, and fats, because it is a utilizable source of energy which is not stored. Vitamins may be added to the alcohol solution without rendering the vitamins inactive (10).

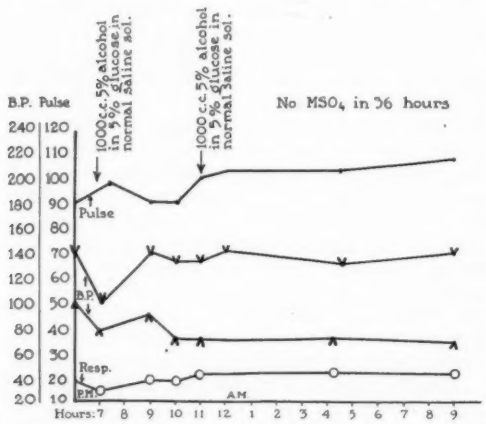

B.P. Pulse
1000 c.c. 5% alcohol in 5% glucose in normal saline sol.
1000 c.c. 5% alcohol in 5% glucose in normal saline sol.
No MSO_4 in 36 hours
Pulse
B.P.
Resp.
P.M.
A.M.
Hours: 7 8 9 10 11 12 1 2 3 4 5 6 7 8 9

Chart 2. Abdominoperineal operation—1000 cubic centimeters of 5 per cent alcohol in glucose during surgery.

The sedative and analgesic qualities of the 5 per cent alcohol solutions are very dramatic (4, 10). With spinal anesthesia, which is used in 22.2 per cent of our urological surgical cases, we have employed 5 per cent alcohol as a supplement during the entire operative procedure. Patients who have this form of medication, doze, relax, lose all apprehension, and often have no memory of the surgical interlude. Postoperatively, the 5 per cent alcohol solution has been continued with the most gratifying results. The use of an opiate or other sedative may be eliminated entirely if the rate of flow of the intravenous alcohol is regulated to the patient's needs. We do not permit more than 3000 cubic centimeters of the 5 per cent alcohol over a 24 hour period. We usually find 1000 to 2000 cubic centimeters adequate.

The value of intravenous alcohol in postoperative recovery is twofold. Not only is it given as a sedative and analgesic, but as a safeguard against the possibility of atelectasis and other pulmonary complications. The respiratory rate and tidal exchange remain the same or are increased (5, 6).

The vasodilatory effects of alcohol suggested its use in the cardiac patient (5, 13). In 5 per cent and 10 per cent solutions, it is beneficial in patients troubled with heart diseases. It increases the dilatation of the blood vessels and possibly the coronary arteries, so that even though fluids are given intravenously, the blood pressure is not significantly increased. In cardiacs, one may use a 10 per cent solution of alcohol, thereby decreasing the actual amount of fluid intake necessary to maintain the required caloric intake.

In the debilitated and morbid patient we have eased restlessness and pain. In the cancer patient who has previously been made comfortable with fluids and morphine, we have markedly reduced the necessity for opiates. In the alcoholic, who is approaching or has developed delirium tremens due in part to the sudden withdrawal of his customary alcoholic intake, we have been successful in controlling him with intravenous alcohol when all other medications in the usual dosages have failed.

The complications that have occurred from the intravenous infusion of 5 per cent or 10 per cent alcohol have been minor. Occasionally, when the fluid had been given too rapidly, there has occurred restlessness and inebriation. It is singular that few cases have needed restraint. The infusion can be discontinued or slowed, with the resultant return to the quiet state of well-being. Occasionally the administration has been complicated by the sclerosed vessel. This occurs more frequently with the 10 per cent than the 5 per cent solution. We have had one partial ulnar nerve paralysis which may have been caused by subcutaneous alcohol in the cubital fossa. Because of this occurrence, we suggest the use of blood vessels other than those in the cubital fossa, and recommend that the beginner at venipuncture use saline for the cannulation of the needle before changing to alcohol. In numerous cases the alcohol has run subcutaneously without causing symptoms other than slight discomfort. This has been relieved by warm, moist applications.

SUMMARY

1. Five per cent and 10 per cent alcohol intravenously increases the caloric intake and has special value in those cases with inanition.

2. It is a potent sedative and analgesic, and can be substituted for the opiates and other forms of sedation.

3. Sedation is not attended with depressed respiration.

4. It may be used in cardiac patients with relative safety because of its vasodilatory effect and minimal effect on the blood pressure.

5. It has a definite place in regional anesthesia as a supplement during the operative procedure.

6. It has proved its value in alcoholic patients who cannot be controlled with the usual doses of narcotics.

7. At the present we have found no contraindications.

REFERENCES

1. Adams, R. C. Intravenous Anesthesia. New York: Paul B. Hoeber, Inc., 1944.
2. Atwater, W. D., and Benedict, F. G. Mem. Nat. Acad. Sc. U. S., 1902, 8: 235–395.
3. Coffey, R. R. Missouri M. Ass., 1941, 38: 6, 188.
4. Craddock, F. H., and Craddock, F. H., Jr. J. M. Ass., Alabama, 1942, 12: 134–137.
5. Goodman, L., and Gillman, A. The Pharmacological Basis of Therapeutics. New York: The Macmillan Co., 1941.
6. Higgins, H. L. J. Pharm. Exp. Ther., 1917, 9: 441–472.
7. Jetter, W. W. Am. J. M. Sc., 1938, 196: 475–487.
8. Mellanby, E. Brit. M. Res. Com. Spec. Report, 1919, Series 31, 1–48.
9. Miles, W. R. J. Pharm. Exp. Therap., 1922, 20: 265–319.
10. Mueller, Sterling. Surg. Clin. N. America, April 1939, 19: 401–405 (New York Number).
11. Newman, H. W., Lehman, H. J., and Cutting, W. C. J. Pharm. Exp. Therap., 1938, 62: 301–306.
12. Stoe, Caleb S., Jr. Virginia Mason Hospital Clin., 1941, 20: 3, 58.
13. White, P. D., and Sharker, T. J. Am. M. Ass. 1934, 102: 655–657.

THE INFLUENCE OF THYROIDECTOMY ON THE PROMINENCE OF THE EYES IN THE GUINEA PIG AND IN MAN

BROWN M. DOBYNS, M.D., Rochester, Minnesota

ONE of the most perplexing problems in the field of physiology of the thyroid gland is the relationship of exophthalmos to thyroid disease. Why an occasional patient with exophthalmic goiter experiences an increase in exophthalmos after thyroidectomy while the great majority of patients appear to have been benefited presents a question.

Careful study has been made of the changes in prominence of the eyes of experimental animals and of patients after thyroidectomy. With regard to patients, efforts have been made to discover the relationships between the clinical features of thyroid disease and the demonstrable changes in the eyes after thyroidectomy. The studies of guinea pigs evolved from other experimental studies in which it was found that it was impossible to establish a definite, constant eye reading with regard to prominence of the eyes in guinea pigs after thyroidectomy. The eyes seemed to be increasing in prominence.

ANIMAL EXPERIMENTATION

A review of the literature revealed a difference in opinion regarding the effect of thyroidectomy on prominence of the eyes of experimental animals. Some investigators have reported a noticeable increase in prominence in different species (8, 28). Others failed to find this change (1, 2, 10). It has been shown that proptosis in guinea pigs is produced more easily with thyrotropic hormone after thyroidectomy has been performed than in guinea pigs that have not been thyroidectomized (1, 2, 5, 6, 13). Furthermore, one investigator (7) has demonstrated that proptosis, similarly produced in guinea pigs that have not been subjected to the thyroidectomy, does not become apparent until the animals have become refractory to the thyrotropic preparation and their basal metabolic rates have begun to decline. Finally, it has been shown that proptosis can be produced with methyl cyanide much more easily after thyroidectomy (17, 18) than if thyroidectomy has not been performed.

Probably the best explanation for the differences in opinion regarding the effect of thyroidectomy on the prominence of the eyes of experimental animals is that investigators had no very reliable means of measuring exophthalmos. The earliest methods consisted of studying animals in pairs and comparing their gross appearances (11–18). More recently measuring devices placed on the head and even on the corneal surfaces have been used (20–25). A camera lucida (1, 2) method has been used to avoid touching the cornea. In these methods, however, rather vigorous restraints were required; a fact which may contribute to error. The necessity for more accurate methods of measuring proptosis in animals becomes apparent.

EXPERIMENTAL METHODS

Two improved methods, about equally accurate, have been devised for measuring exophthalmos in guinea pigs. In the first method calipers were used to measure the intercorneal distance. An animal was placed beneath the frame (Fig. 1) and, by sighting through the peep-sights above the animal's head, the blades of the calipers could be arranged in line with the corneal surfaces on the two sides without touching the animal. The set distance between the peep-sights depended on the average size of the heads of the group of guinea pigs to be studied.

The second method involved the use of the camera lucida (Fig. 2). The guinea pig was placed in a trough equipped with a sliding floor which could be moved forward until the head of the animal was a given distance from the camera lucida. This distance was determined by a fixed rod (Fig. 2, *d*). By looking through the aperture of the camera lucida the image of the animal's head could be seen on a plane which carried a sliding scale (Fig. 2, *a*). The scale was so arranged

From the Division of Surgery, Mayo Foundation.

Abridgement of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

The experimental work was done in the laboratory of Dr. George M. Higgins, at the Institute of Experimental Medicine; the clinical work under the guidance of Dr. Samuel F. Haines.

Presented before the Society for the Study of Internal Secretions, Chicago, June 12, 1944.

that 10 centimeters at the position of the animal's head was equal to 10 centimeters on the sliding scale. Thus, the intercorneal distance could be measured without touching the animal.

It was found that if the animals were placed in the dark for 20 minutes preceding the measuring procedure and then were exposed to the bright light associated with the measuring device, many of them froze into a rigid position. This state, when acquired, eliminated the necessity of forced restraint and greatly reduced the errors incident to measuring the degree or extent of proptosis.

Because these methods proved essentially equal in accuracy, both were used in the experiments which form the basis of this report. Measurements were obtained on each animal three times with each method each day they were observed. The average of these six determinations was accepted as the status of the prominence of the eyes for that particular day. The accuracy of these methods was tested by study of several normal guinea pigs, the water balance and salt intake of which were modified. Comparatively slight changes in body weight, due to hydration, were accompanied by parallel changes in prominence of the eyes (Fig. 3).

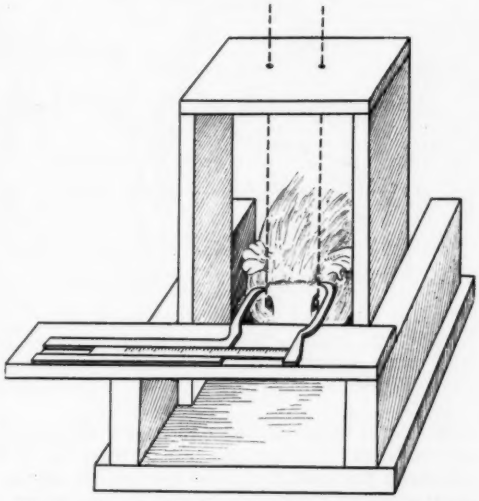


Fig. 1. Improved caliper method of measuring intercorneal distance.

EXPERIMENTAL PROCEDURE AND RESULTS

With these methods of measuring exophthalmos, which were somewhat more accurate than methods previously devised, an experiment to determine the effect of thyroidectomy on the prominence of the eyes of guinea pigs was undertaken. Seventeen normal male pigs, weighing from 325 to 500 grams were selected for their susceptibility to the measuring procedure. Thir-

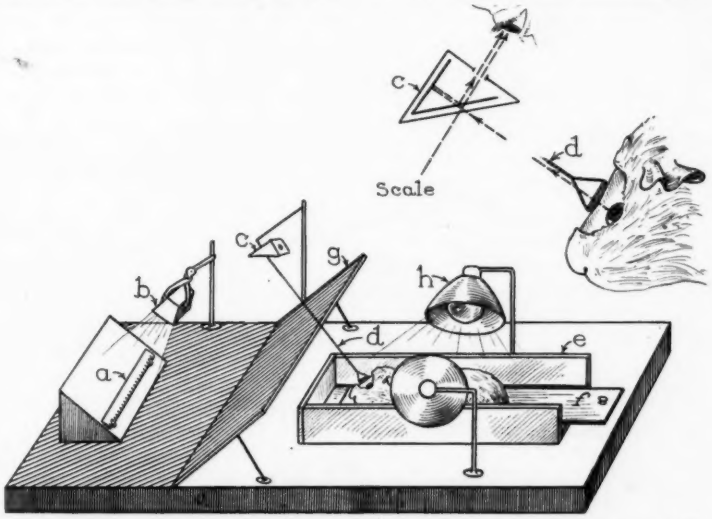


Fig. 2. The camera lucida method of measuring the intercorneal distance. *a*, millimeter scale; *b*, daylight blue microscope lamp; *c*, camera lucida; *d*, distance rod, to control distance between camera lucida and head of animal; *e*, trough to hold animal; *f*, sliding floor; *g*, light shield; *h*, lights to illuminate animal.

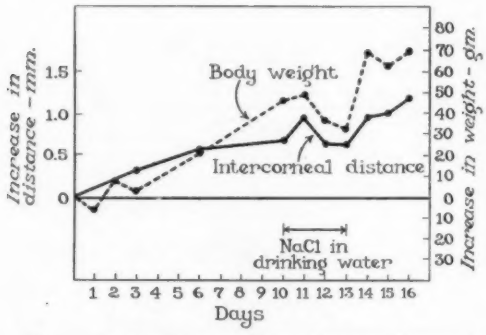


Fig. 3. To illustrate parallelism between changes in body weight and prominence of the eyes of a growing, normal animal.

teen were thyroidectomized and 4 served as normal controls. The prominence of the eyes was measured preoperatively and postoperatively at intervals of 1 to 4 days. Changes in body weight also were determined.

The results of the experiment are illustrated (Fig. 4). It was found that although the thyroidectomized animals failed to increase in body weight, prominence of the eyes did increase. This increase in proptosis was out of proportion to the slight increase which was demonstrated by the normal animals that had gained much more weight.

Thus it can be seen (Fig. 5) that it is important to determine the increase in width that takes place in that portion of the skull which lies between the orbits. The supraorbital notches of the guinea pig's skull lie above the medial boundaries of the orbits. Fortunately these notches are just beneath the skin and thus are easily located with the blades of appropriate calipers. It is therefore possible to measure the distance between the supraorbital notches in exactly the same way on several successive occasions. Changes in distance between the supraorbital notches (*a* in Fig. 5) must be deducted from the change in intercorneal distance (*b*) in order to obtain a true evaluation of the proptosis. The determination in this way of the changes in width of that portion of the skull which lies between the orbits served as a control.

In the lower right portion of Figure 4, measurements of the frontal bones made by this method are illustrated. In the thyroidectomized animals, there was not much increase in width of that portion of the skull which lies between the orbits; this is in keeping with the slight changes in body weight of these animals. On the other hand, in the normally growing controls, there was somewhat more increase in this measurement of the skull. When these skull measurements are deducted from the changes in the intercorneal distance, emphasis is added to the already established fact that thyroidectomy results in increase in prominence of the eyes.

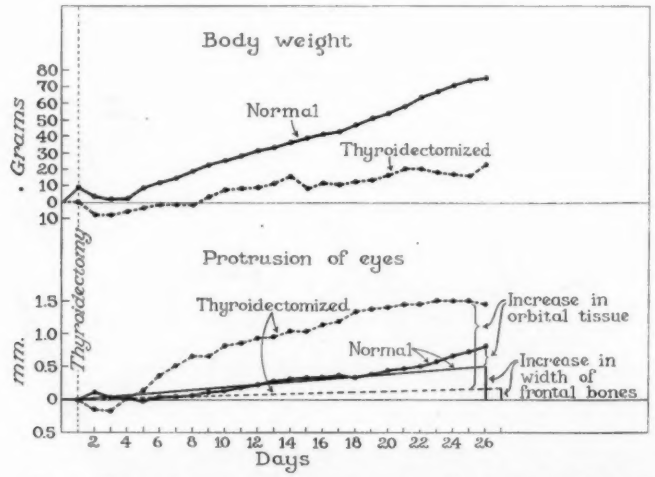


Fig. 4. Changes in the prominence of the eyes resulting from thyroidectomy performed on the normal guinea pig. The increase in the width of the frontal bones, as illustrated in the lower right portion of the graph, is represented by the same scale as the measurements dealing with the eyes.

TABLE I.—CHANGES IN PROMINENCE OF EYES OF PATIENTS WITH EXOPHTHALMIC GOITER OR ADENOMATOUS GOITER FOLLOWING SUBTOTAL THYROIDECTOMY

	Exophthalmic		Adenomatous	
	No.	Per cent	No.	Per cent
Total cases	98		135	
Decreased or remained the same	3	3	6	4
Increased 0.25 to 1.25 mm.	31	31.6	50	37
Increased 1.25 to 2 mm.	29	29.6	46	34
Increased 2 mm. or more	35	35.7	33	24

This increase in proptosis is in all probability due to an increase in the retrobulbar tissues, for it is well recognized that changes in the globe are negligible. Six of the 13 thyroidectomized animals were killed at the conclusion of the experiment. Histologic studies of the tissues revealed minimal edema of the retrobulbar tissues in 3 of the 6 instances. Smelser (25) has shown by analytical methods that there is a slight increase in the water content of orbital fat of guinea pigs after thyroidectomy.

CLINICAL OBSERVATIONS

The reports in the literature dealing with this problem as it relates to patients disagree. Bartlett (3, 4), in discussion of other papers, declared that prominence of the eyes of patients increased after thyroidectomy but he failed to present any data to support his contention. Grace and Weeks reported that prominence of the eyes of their

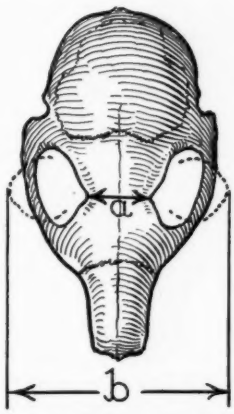


Fig. 5. Skull of guinea pig. *a*, distance between supraorbital notches; *b*, intercorneal distance.

series of patients did not increase after thyroidectomy. Their measurements were made with an exophthalmometer. When and how frequently they made measurements is not certain. Soley (26, 27) reported that the prominence of the eyes increased after thyroidectomy for exophthalmic goiter or adenomatous goiter with hyperthyroidism.

The present investigation deals with 233 consecutive patients who underwent thyroidectomy. The Hurthle exophthalmometer was used. Measurements were made preoperatively and at intervals of 1 to 4 days postoperatively. The shortest period of observations was 14 days. The exophthalmos was measured six times on each day that

TABLE II.—A TYPICAL RECORD, ILLUSTRATING THE INCREASE IN PROMINENCE OF THE EYES FOLLOWING THYROIDECTOMY* IN A CASE OF EXOPHTHALMIC GOITER†

Relation to operation, days	Measurements, mm. ‡						Body weight		Basal metabolic rate, per cent
	Right eye			Left eye			Pounds	Kg.	
16th preoperative									+46
Operation §	13.0	12.5	12.5	13.5	13.0	13.0	120	54	
3rd postoperative	13.5	13.5	13.5	13.5	13.5	13.5			
5th postoperative	13.5	14.5	14.0	13.5	14.0	13.5			
9th postoperative	14.0	14.0	14.0	14.0	14.5	14.0	122	55	
12th postoperative	14.5	14.5	14.5	14.0	14.5	14.5	123	56	
16th postoperative	14.5	14.5	14.5	14.5	14.0	14.5	124½	56	+2
19th postoperative	15.0	15.0	15.5	15.0	15.0	15.0	125	57	
23rd postoperative	15.5	15.5	16.0	16.0	15.5	15.5	125	57	

*Thyroidectomy, in this case, consisted of subtotal resection, leaving in place ¼ of each lobe of the thyroid gland. The right inferior thyroid artery was ligated.

†Pathologic diagnosis based on the 36 gm. of tissue removed was diffuse parenchymatous hypertrophy.

‡Exophthalmometer setting, 103.

§Readings were made before the operation on this day. The day of operation is counted, at the Mayo Clinic, as the first postoperative day

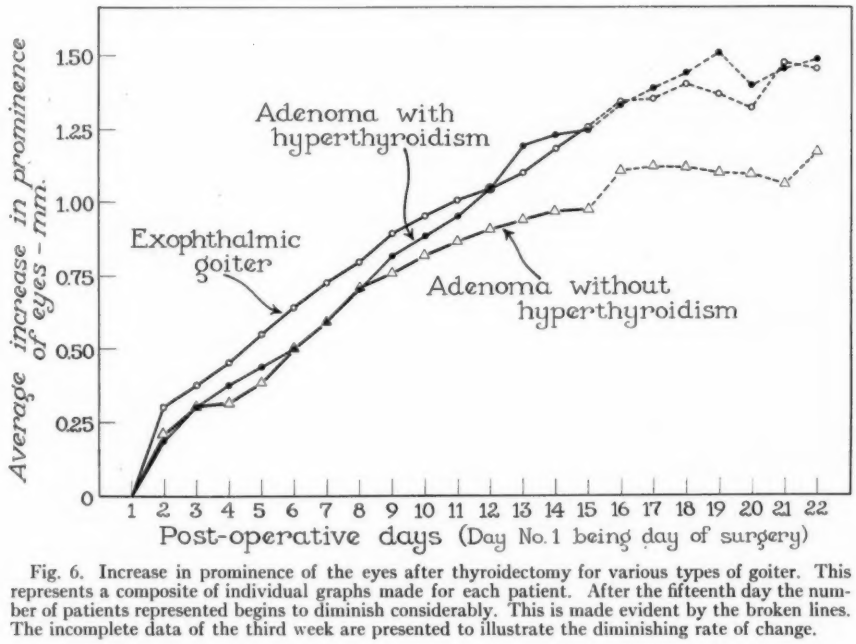

Average increase in prominence of eyes - mm.
1.50
1.25
1.00
0.75
0.50
0.25
0
Adenoma with hyperthyroidism
Exophthalmic goiter
Adenoma without hyperthyroidism
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
Post-operative days (Day No. 1 being day of surgery)

Fig. 6. Increase in prominence of the eyes after thyroidectomy for various types of goiter. This represents a composite of individual graphs made for each patient. After the fifteenth day the number of patients represented begins to diminish considerably. This is made evident by the broken lines. The incomplete data of the third week are presented to illustrate the diminishing rate of change.

observations were made, three times on each eye. The average of the six measurements represented the observations for the day. Great care was taken to make the measurements in the same way and under the same conditions at all observations. In the course of the investigation, a little more than 10,000 exophthalmometer readings were made, and in this large number of readings it seems reasonable to assume that variations in the technique of making the measurements were reduced to a minimum. The importance of making the measurements at the same time after the patient's arising was recognized. Importance also was attached to having the eyes in the same position at each measurement. This was accomplished by having the subject look, with the right eye, at the observer's right ear and, with the left eye, at the observer's left ear so that the same point on the cornea was observed each time.

The eyes of all but 9 of the 233 patients, regardless of pathologic state, increased in prominence following thyroidectomy. However, the increase in 81 cases, or approximately one-third of them, was 1 millimeter or less, which is negligible.

Physiologically, exophthalmic goiter and adenomatous goiter are different (19). Therefore, it seems reasonable to consider separately the two groups of patients representative of these diseases. The distribution of the patients, according to the different degrees of ocular prominence that developed, is given in Table I. It is evident that of the patients whose eyes increased in prominence, about one-third fell in each of the categories set down in the table. The greatest average increase in prominence of the eyes among the patients with adenomatous goiter was 4 millimeters and, among the patients with exophthalmic goiter, it was 3.5 millimeters. A typical record of a patient with exophthalmic goiter is presented in Table II to illustrate the value of the multiple readings mentioned, and the gradual change in prominence of the eyes that is demonstrable in this manner.

The course of events with reference to the eyes of each of the 233 patients was plotted individually and the composite of these records is presented in Figure 6. It has been found that prominence of the eyes of the patients who had adenomatous goiter with hyperthyroidism or exophthalmic goiter was more greatly increased after thyroidectomy than was that of patients who had adenomatous goiter without hyperthyroidism. Because of the volume of data on which this report is based, this difference is probably significant.

Control observations were made on 16 patients, 8 of whom underwent surgical procedures which

TABLE III.—CHANGES IN THE EYES FOLLOWING SURGICAL PROCEDURES OTHER THAN THOSE ON THE THYROID GLAND

Change in prominence of eyes			
Decrease from 0.5 to 1 mm.	No change to 1 mm. increase	Increase of 1.25 mm.	Increase of more than 1.25 mm.
6 cases (in 5 of 6, abdomen was opened)	9 cases (in 2 of 9, abdomen was opened)	1 case (parathyroid tumor)	0 cases

were confined to the region of the neck but were not for thyroid disease. The other 8 patients were subjected to procedures which required opening of the abdominal cavity. Among these patients, contrary to the findings after surgical operation on the thyroid gland, was a group of 6 whose eyes decreased in prominence after the operations (Table III). Five of the 6 were patients whose abdominal cavities were opened and whose fluid balance probably was disturbed after operation. Nine of the 16 patients fell into the group in which prominence of the eyes after operation ranged from no increase up to an average increase of 1 millimeter. That increase has been regarded as negligible. In the 1 case in which the average increase was 1.25 millimeters a parathyroid tumor had been removed. In this case it was necessary to interrupt a considerable part of the blood supply of the thyroid gland and to mobilize both of its lobes in order to discover and remove the parathyroid tumor that was lying posterior to the thyroid.

Since the data suggested that prominence of the eyes increases after thyroidectomy, it seemed reasonable to evaluate the increase in terms of the other clinical features of thyroid disease. Since this study suggests that there is a correlation between the change in basal metabolic rate and the change in prominence of the eyes, this and various other correlations will be considered, first with reference to exophthalmic goiter.

It was found among the patients with exophthalmic goiter that if the initial basal metabolic rate was relatively high, the increase in prominence of the eyes following thyroidectomy was in some cases relatively striking. However, although this was statistically significant, it was scarcely impressive.

A more significant correlation was found between the change in prominence of the eyes and the fall in the basal metabolic rate which resulted from operation. The cases of exophthalmic goiter were divided into two groups in relation to the magnitude of the postoperative fall in basal metabolic rate; namely, those in which the fall

TABLE IV.—THE FALL IN THE BASAL METABOLIC RATE AS RELATED TO CHANGES IN PROMINENCE OF THE EYES FOLLOWING OPERATION FOR EXOPHTHALMIC GOITER

Decrease in basal metabolic rate				
	Per cent			
	Less than 30		More than 30	
	No.	Per cent	No.	Per cent
Increase of 1 mm. or less	15	54	16	28
Increase of 1.25 to 2 mm.	8	28	16	28
Increase of 2 mm. or more	5	18	25	44
Total cases	28		57	

was less than 30 per cent and those in which it was more than 30 per cent. The patients whose basal metabolic rates fell slightly were inclined to relatively slight increase in prominence of the eyes, whereas those whose basal metabolic rates fell markedly were inclined to relatively great increase in prominence of the eyes (Table IV).

Still considering exophthalmic goiter, a study of the relation of preoperative exophthalmos to the postoperative change in prominence of the eyes was made. There was no correlation between presence or absence of preoperative exophthalmos and postoperative increase in prominence of the eyes.

Cognizance was taken of the presence of thyroiditis in those cases in which a pathologic diagnosis of parenchymatous hypertrophy of the thyroid gland was made. Thyroiditis was recognized as consisting of more than the casual scattering of lymphocytes usually seen in the thyroid gland in cases of exophthalmic goiter. There was no correlation between the presence of thyroiditis in association with exophthalmic goiter and change in prominence of the eyes after surgical treatment. It has been recognized in the Mayo Clinic, however, that in surgical cases of exophthalmic goiter in which extreme degrees of thyroiditis exist, hypothyroidism is more likely to develop relatively late in the postoperative course than it is in cases in which there is no thyroiditis. The presence of thyroiditis, therefore, may be correlated with changes in prominence of the eyes that are found relatively long after operation.

The weight of the thyroid tissue removed in the case of exophthalmic goiter is a relative estimate of the total weight of the gland. The weight of the tissue removed in the cases of exophthalmic goiter was determined and studied in the light of the

postoperative changes in the eyes. The data suggest that there is no clear-cut correlation between the weight of the thyroid gland and the increase in prominence of the eyes after operation. The sex of the individual likewise had no relation to the postoperative change in prominence of the eyes in cases of exophthalmic goiter.

Now, leaving exophthalmic goiter, clinical and pathologic features in cases of adenomatous goiter were studied with regard to changes in prominence of the eyes which followed thyroidectomy. Those patients who had adenomatous goiter associated with hyperthyroidism were more inclined to develop a striking increase in prominence of the eyes after thyroidectomy than were patients who had adenomatous goiter not associated with hyperthyroidism. The difference in these two types of adenomatous goiter was slight but definite in view of the large number of observations (Fig. 6).

Attempts to estimate the amount of thyroid tissue remaining after removal of adenomas were unsatisfactory.

The presence of intra-adenomatous hypertrophy had no relation either to the changes in prominence of the eyes or to the preoperative basal metabolic rate.

DISCUSSION

It has been demonstrated that there is an increase in prominence of the eyes during the first 3 weeks following subtotal thyroidectomy. This confirms the findings of Soley (26, 27). The question arises as to what the outcome of this ocular change may be. Obviously, if the increase continued indefinitely at the same rate, it long would have been a recognized clinical fact. At the time of writing of this report, 14 patients had been seen 2 or more months after thyroidectomy and, for the most part, the increase in ocular prominence that previously had been demonstrated had not regressed.

Correlation was found between the fall in the basal metabolic rate and the increase in prominence of the eyes in cases of exophthalmic goiter after thyroidectomy. Although comparatively few of the patients were followed subsequent to the period of 3 weeks of observation, those who have been followed have given evidence of a similar correlation. Nine out of 10 of those who have been seen several months after surgical treatment, and whose basal metabolic rates have fallen even more than at the end of the period of 3 weeks, have demonstrated further increase in prominence of their eyes. It is of further interest that most of such patients who have received thyroid extract have shown a regression in the prominence of the eyes as the basal metabolic rate has returned to normal. Since the indications are that fall in basal metabolic rate subsequent to the short period of observation covered by most of this study is accompanied by further increase in prominence of the eyes, thyroiditis (lymphocytic infiltration of the thyroid) and its predisposition to postoperative hypothyroidism may have some bearing on changes in the eyes.

Thirteen patients who have sought treatment for myxedema either of postoperative or spontaneous origin gave evidence of regression in the prominence of their eyes when thyroid extract was administered to raise their basal metabolic rates.[1] This phenomenon seemed more noticeable among those patients who had suffered from their hypothyroidism for a relatively short period of time.

To the casual observer, almost all of the patients described in this study have seemed to show gross improvement in prominence of their eyes after thyroidectomy. I am impressed by the fact that there is a distinction between actual prominence of the eyes and the other numerous eye signs, such as retraction of lids, stare, tension of the muscles of expression and so on, which contribute to the exophthalmic appearance. It seems, therefore, that it is improvement in these latter signs which mask the actual increase that takes place in prominence of the eyes after thyroidectomy for exophthalmic goiter.

In accepting the observations on basal metabolic rate in cases of exophthalmic goiter, it is important to recognize that many of the patients had been subjected to varying degrees of treatment with iodine before presenting themselves for treatment at the clinic. The initial basal metabolic rate, therefore reflected varying degrees of iodinization with its accompanying influence on metabolism.

No patient in this series, up to the time of writing of this report, had been recognized as presenting "progressive postoperative exophthalmos" or "malignant exophthalmos," which has been the subject of important studies by Naffziger and others. Prominence of the eyes of one patient has increased as much as 4 millimeters but the patient did not appear to be exophthalmic.

SUMMARY

Observations have been made on the changes in the prominence of the eyes after total thyroidectomy performed on 13 guinea pigs and after subtotal thyroidectomy performed on 233 patients. An improved caliper method and a camera lucida method have been devised and found more

[1] Unpublished work.

accurate than some previous methods for studying such changes in experimental animals. Multiple readings were made on the animals with these instruments and more than 10,000 exophthalmometer readings were made on patients. Increase in prominence of the eyes of both experimental animals and of patients was found. Among patients there apparently was some correlation between the fall in basal metabolic rate and the increase in the prominence of the eyes. The presence of thyroiditis, the sex of the patient, the weight of the thyroid tissue removed, the presence of intra-adenomatous hyperplasia and the presence of preoperative exophthalmos apparently had little or no correlation with the changes in prominence of the eyes after subtotal thyroidectomy performed on patients.

REFERENCES

1. Aird, R. B. Arch. Ophth., Chic., 1940, n.s. 24: 1167–1174.
2. Idem. Ann. Int. M., 1941, 15: 564–581.
3. Bartlett, W., Jr Surg. Gyn. Obst., 1940, 71: 450–453.
4. Idem. Discussion. Tr. Am. Ass. Goiter, 1941, 145–146.
5. Friedgood, H. B. Bull. Johns Hopkins Hosp., 1934, 54: 48–74.
6. Idem. Tr. Am. Ass. Goiter, 1941, 128–142.
7. Idem. J. Clin. Endocr., 1941, 1: 804–812.
8. Gley, E. C. rend. Soc. Biol., 1910, 68: 858–861.
9. Grace, R. V., and Weeks, C. Ann. Surg., 1941, 113: 496–505.
10. Lambie, C. G. Med. J. Australia, 1939, 2: 819–830 (pt. 1); 853–869 (pt. 2).
11. Marine, David. Tr. Internat. Coll. Surgeons, 1938, 1: 55–62.
12. Idem. Ann. Int. M., 1938, 12: 443–453.
13. Marine, David and Rosen, S. H. Proc. Soc. Exp. Biol., N.Y., 1933, 30: 901–903.
14. Idem. Am. J. M. Sc., 1934, 188: 565–571.
15. Idem. Proc. Soc. Exp. Biol., N.Y., 1936, 35: 354–356.
16. Idem. Am. J. Physiol., 1938, 121: 620–624.
17. Marine, David, Rosen, S. H. and Cipra, Anna. Proc. Soc. Exp. Biol., N.Y., 1933, 30: 649–651.
18. Marine, David, Spence, A. W. and Cipra, Anna. Proc. Soc. Exp. Biol., N.Y., 1932, 29: 822–823.
19. Mayo, C. H., and Plummer, H. S. The thyroid gland. (The Beaumont Foundation Lectures.) St. Louis: C. V. Mosby Co., 1926.
20. Paulson, D. L. Proc. Mayo Clin., 1939, 14: 828–830.
21. Idem. Unpublished data.
22. Smelser, G. K. Am. J. Anat., 1943, 72:149–169.
23. Idem. Anat. Rec., 1943, 85: 245–259.
24. Ibid., 86: 41–57.
25. Idem. Am. J. Physiol., 1943, 140: 308–315.
26. Soley, M. H. Arch. Int. M., 1942, 70: 206–220.
27. Idem. California West. M., 1944, 60: 64–68.
28. Vincent, S., and Jolly, W. A. J. Physiol., Lond., 1904, 32:65–86.

TOTAL GASTRECTOMY

Report of Eight Cases

T. E JONES, M.D., F.A C.S., and R. W. KEHM, M.D., Cleveland, Ohio

IN the past many patients with extensive gastric lesions have been said to be surgically incurable and thus have been deprived of the benefits of total gastrectomy because of the prohibitive operative mortality. The procedure should be limited to those patients in whom the lesion is too extensive or too close to the esophagus to make subtotal gastrectomy feasible; then it is the only alternative. Refinement of technique and increased operative ability with a resultant decrease in mortality have rendered total gastrectomy practicable in selected cases. Until 1929 the mortality rate in all cases of total gastrectomy reported in the literature was 53.8 per cent, according to Finney and Rienhoff. Recently, Coller and associates (2) reported only 2 deaths in 19 cases, or a mortality of 10.5 per cent. Our series of 8 consecutive cases was without operative mortality.

The history of total gastrectomy is adequately discussed in the literature by Walters, Finney and Rienhoff, Roeder, Lahey, and others. Schlatter is generally credited with the first successful total gastrectomy in 1897, his patient living for 1 year and 53 days. Roeder found only 88 authenticated cases reported up to 1933. Since then the increase in reported cases shows a definite trend toward this procedure in selected cases.

INDICATIONS

Total gastrectomy is particularly adaptable for the linitis plastica type of stomach. However, it is also indicated in neoplasms extending into the cardiac end of the stomach and, even in deep penetrating ulcers located high in the stomach and therefore, not amenable to medical management or to subtotal gastrectomy.

In the 8 consecutive cases of total gastrectomy presented here, operation was performed since March, 1943. Three patients had localized ulcerating carcinomas, high in the stomach; in 2, extensive infiltrating neoplasms involved most of the stomach; 2 patients had persistent penetrating benign ulcers high in the cardia; in 1 patient with multiple lymphosarcomatous lesions of the stomach a single tumor was located only 1 inch from the esophageal orifice. Pertinent information concerning these cases is summarized in Table I.

From the Cleveland Clinic.

The symptoms in all cases were unbearable and consisted chiefly of pain, obstructive symptoms, or both. In Cases 4 and 7 chronic, intractable ulcers caused acute penetrating pain. Each patient had extensive medical management without relief and welcomed surgical intervention. Operation was undertaken to provide relief from symptoms and to enable the patient to live some months or years of fairly comfortable, productive life.

OPERATIVE TECHNIQUE

Technically total gastrectomy is a most difficult procedure, requiring adequate exposure, mobility, and some degree of mechanical skill. Experimental work, such as that of Mann (7), who had only 3 survivals in a large group of dogs, substantiates these difficulties. We believe that certain features in the operative technique in our series contributed to the success of the operation and deserve mention.

1. The use of spinal anesthesia in all cases, since it offers ideal operative conditions resulting in the best relaxation and exposure. In addition it enables the patient to co-operate in the immediate postoperative period when forced coughing may abort an incipient atelectasis.

2. The use of an upper midline incision in preference to any other, because it enables the surgeon to work to the right or left with equal facility and results in primary healing without herniation.

3. The removal of the stomach, since the esophagojejunostomy anastomosis is thus made easier than when the stomach is left intact and used as a retractor to pull down the esophagus for suture. The use of only two layers of suture for anastomosis—a continuous external layer of medium silk (first applied posteriorly) and a mucosal layer of chromic catgut.

4. The dissection of a shelf of diaphragmatic peritoneum which is resutured to the jejunum below the line of anastomosis and thus acts as a suspensory to relieve the suture line of some stress.

5. The insertion of the loop of jejunum through the transverse mesocolon. This was not possible in 1 patient who had x-ray therapy years before, and multiple adhesions prohibited the posterior operation.

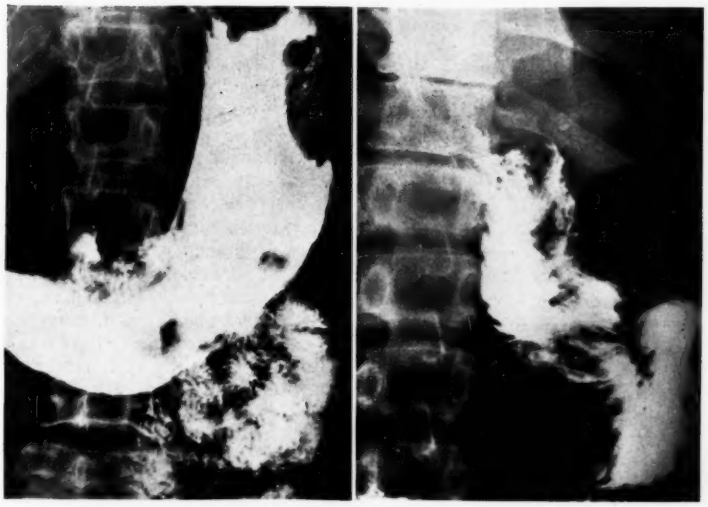


Fig. 1. Multiple lymphosarcomatous lesions of the stomach. Postoperative films showing normal esophageal markings with no obstruction to flow of barium. Intestinal loops empty rapidly with normally functioning enteroenterostomy.

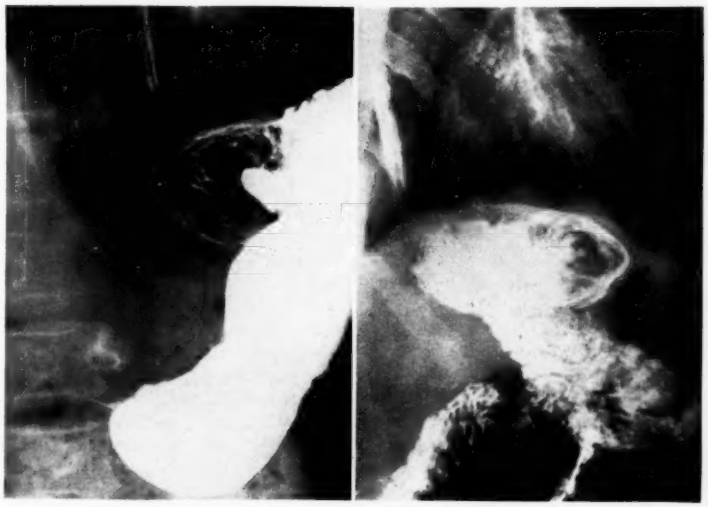


Fig. 2. Peptic ulcer high in cardia along lesser curvature. Clinical impression was malignant lesion, but microscopic studies proved it to be benign. Postoperative films showing excellent functioning of anastomosis without obstruction.

6. The creation of an enteroenterostomy between the afferent and efferent loops of jejunum in order to allow the pancreatic enzymes and biliary secretions to bypass the esophagus and prevent regurgitation.

7. The closure of the wounds with interrupted steel alloy sutures, which in our experience minimizes wound infections and their undesirable sequelae.

8. The mobilization of the left lobe of the liver

TABLE I.—SUMMARY OF 8 CASES REPORTED

Case Age Sex	Pathologic condition present	Postoperative complications	Postoperative hospital stay in days	Mortality
1 44 M	Infiltrating carcinoma of middle third of stomach with gland metastasis	Partial lobar atelectasis	16	0
2 43 M	Ulcerating neoplasm in lesser curvature 2.3 cm. from esophagus	Small pelvic abscess, diarrhea, steatorrhea	34	0
3 46 F	Infiltrating carcinoma of whole stomach extending to gastrocolic and gastrohepatic omenta	Biliary regurgitation	18	0
4 66 M	Penetrating ulcer 2 by 1.4 cm. located 1 cm. from esophagus on posterior wall	None	16	0
5 60 M	Infiltrating carcinoma of whole stomach and glands in gastrocolic and gastrohepatic omenta	Right lower lobe atelectasis with pneumonitis, steatorrhea	16	0
6 63 F	Multiple lymphosarcomatous lesions, one being 1 inch from esophagus	Partial atelectasis of right lower lobe, steatorrhea	14	0
7 58 M	Penetrating ulcer on lesser curvature 0.5 inch from esophagus	None	14	0
8 48 M	Ulcerating neoplasm of lesser curvature 2 inches from esophagus	None	14	0

by division of the lateral ligament has not been found necessary for exposure.

9. Splenectomy as a routine procedure or to increase exposure does not seem justifiable and is not without danger: Vascular accidents are not uncommon after splenectomy. Splenectomy may be indicated in uncontrollable bleeding from trauma. Splenectomy was performed in 1 case because of extension of malignant lesion into the gastrolienal ligament and perisplenic areolar tissue.

10. The removal of the gastric tube at the completion of the operation in order to prevent pressure necrosis at the line of anastomosis.

Preoperative preparation consists of daily gastric lavage, intravenous saline injections, transfusions when indicated, administration of parenteral vitamins, and a careful determination of renal and cardiac reserve. Gastric lavage is done 2 hours after meals each night. If the gastric residuum is consistently over 200 cubic centimeters, continuous suction is used for 36 hours immediately before operation. Five hundred cubic centimeters of intravenous 3 per cent saline is given each morning until the excretion of urinary chlorides is normal.

After operation only sips of water are given by mouth for 4 or 5 days. Then the patient is gradually started on small amounts of liquid food. Intake is slowly increased so that by the time of discharge the patient is taking a high caloric soft diet. He is instructed to return to normal diet in a few weeks but is cautioned to eat slowly and less at a time and to masticate well. Supportive measures as indicated are given throughout the postoperative period.

In our series postoperative complications, except for Case 2, were relatively mild considering the extensiveness of the procedure. Three cases developed partial atelectasis with associated pneumonitis; all responded to forced coughing, expectorants, and sulfonamide therapy. Case 2 developed a pelvic abscess of pure Streptococcus viridans culture, the source of which could not be ascertained. Drainage and irrigation through a small suprapubic incision were the only treatment necessary.

PHYSIOLOGIC EFFECTS OF TOTAL GASTRECTOMY

In the removal of an organ as vitally important to the physiology of the body as the stomach, certain postoperative physiologic changes must be anticipated. These changes can be conveniently grouped as digestive disturbances and alterations in the hemopoietic system.

The digestive disturbances most commonly encountered are diarrhea, steatorrhea, dysphagia, and biliary regurgitation.

Diarrhea after total gastrectomy is reported frequently. Clute reported 2 out of 3 cases with diarrhea, one of which responded somewhat to dilute hydrochloric acid. In our series only 1 patient, Case 2, developed diarrhea. This symptom began as soon as the patient started to take food orally and persisted for approximately 2 months. It ceased spontaneously and has not recurred to date. Hydrochloric acid was not beneficial. The cause of this diarrhea is difficult to explain. Sudden removal of hydrochloric acid from the upper gastrointestinal tract must be a factor, since reported cases responded to its administration. Ivy showed that enteritis frequently causes death after total gastrectomy in dogs and attributed it to the lack of attenuation of the bacterial flora of the upper gastrointestinal tract. This is undoubtedly a factor, but loss of gastric enzymes must also be involved, since hydrochloric acid does not affect the diarrhea in many cases.

Persistent steatorrhea develops after total gastrectomy. Rekers and others, in a comprehensive study, showed that the fat content of the stools was greatly increased after total gastrectomy and that only pancreatic enzymes consistently restored the fat content of stools to normal. Three cases in our series showed definite evidence of

persistent steatorrhea. Since no careful follow-up survey was possible at the time, the presence of steatorrhea in the 5 other cases could not be established. However, the deficiencies usually seen with persistent steatorrhea or sprue were not present, so that the condition is one of scientific interest rather than of actual disability.

Dysphagia and biliary regurgitation may result from a defective operative procedure, from stricture at the site of anastomosis, or from obstruction in a loop of intestine. No dysphagia developed in this group. Only 1 patient (Case 3) had unexplained, persistent regurgitation especially after eating; roentgenologic studies showed a normally functioning stoma without dilatation of the jejunum and a normal enteroenterostomy.

Alterations in the hemopoietic system after total gastrectomy are to be expected. Castle (11) showed that pernicious anemia is at least partly due to loss of intrinsic factor from the stomach. Yet paradoxical as it may seem, the anemia is usually not pernicious but rather secondary or iron deficiency anemia of the normocytic, normochromic type. Seldom are macrocytic anemias reported. Moynihan's classic case of total gastrectomy was supposedly a victim of Addison's anemia, and Hurst reported 5 cases of this type. Ivy showed that the hemopoietic reserve was severely decreased after total gastrectomy in dogs, so that any increased stress on the hemopoietic system, such as pregnancy or extensive hemorrhage, had a tendency to result in severe anemias of a secondary type and even in death. Iron deficiency anemia is to be expected in these cases, since iron salts are insoluble and therefore not absorbed in an alkaline medium. Table II presents the blood picture in this group of patients. Despite the absence of antianemic therapy, no evidence of anemia was present in these 8 patients. However, periodic blood counts are indicated; and patients must be cautioned about the dangers of increased stress on the blood stream.

TABLE II.—BLOOD PICTURE IN 8 CASES* REPORTED

Case	Hemoglobin %	Red cells in millions	White cells	Color index	Serum proteins
1	.91	4.9	7500	0.92	—
	78	4.2	—	0.92	—
	81	4.1	5800	0.98	—
2	78	4.3	9700	0.90	5.7
	82	4.2	13000	0.97	5.1
	84	4.5	5250	0.93	—
3	87	4.7	7300	0.92	5.1
	81	4.4	12800	0.92	4.8
	—	—	—	—	—
4	85	4.0	5800	1.06	5.5
	87	4.7	9750	0.92	4.8
	82	4.8	5700	0.85	—
5	76	4.0	6250	0.95	4.9
	86	4.5	5050	0.95	5.5
	81	4.8	5800	0.84	5.6
6	75	—	4150	—	4.7
	85	5.4	5150	0.78	4.6
	78	4.3	4800	0.90	5.1
7	87	—	7900	—	5.9
	88	4.6	—	0.95	6.0
	—	—	—	—	—
8	75	—	5000	—	5.2
	63	3.3	6750	0.96	—
	—	—	—	—	—

*Blood counts made before operation, at hospital discharge, and at follow-up visit.

OBSERVATIONS

The number of cases of total gastrectomy presented is too small and the period of observation too short for reliable conclusions regarding the effect of altered physiology and the ability of the patient to compensate for removal of such an important organ. With the exception of patients who develop recurrent malignant growths, these persons should pursue a fairly normal, happy life. Postoperative observation to date has shown no tendency toward spontaneous development of anemia. The diarrhea present in 1 case was self-compensatory, and steatorrhea present in 3 cases produced no deleterious results. These patients eat fairly well and suffer very little *post cibum* discomfort. Their general physical stamina seems no less than in the ordinary postoperative case. The men in this group returned to their daily occupations; one is a farmer, who is able to perform manual labor. Even in those cases in which extensive neoplasms are present and the hope for cure is slight, total gastrectomy provides palliation and some months of fairly comfortable life.

Total gastrectomy is of extreme scientific interest and will open new fields for experimental physiologists. Why don't these patients develop pernicious anemia if the intrinsic factor is necessary in hemopoiesis? Why is the removal of the stomach followed invariably by steatorrhea and occasionally by diarrhea? What digestive disturbances follow loss of gastric enzymes? These questions are waiting for answers. Careful analysis and follow-up of the cases of total gastrectomy in human beings may supply answers that will alter our conception of gastrointestinal physiology.

SUMMARY

1. Eight consecutive cases of total gastrectomy are reported. These patients are all living, the postoperative period varying from 6 to 18 months.

2. Refinement of technique and increased operative ability have made the procedure practicable

in selected cases through considerable decrease in mortality.

3. An evaluation of the procedure is not possible at this time because of the limited number of cases presented and the short period of postoperative observation.

4. Explanation of the digestive disturbances and alterations in the hemopoietic system following total gastrectomy may alter our conception of gastrointestinal physiology.

REFERENCES

1. Clute, H. M. Surg. Clin. N. America, 1934, 14: 1039–1048.
2. Farris, J. M., Ransom, H. K., and Coller, F. A. Surgery, 1943, 13: 823–833.
3. Finney, J. M. T., and Rienhoff, W. F., Jr. Arch. Surg., 1929, 18: 140–162.
4. Hurst, A. F. Brit. M. J., 1924, 1: 93–100.
5. Ivy, A. C., Morgan, J. E., and Farrell, J. I. Surg. Gyn. Obst., 1931, 53: 611–620.
6. Lahey. See Clute (1).
7. Mann. See Finney and Rienhoff (3).
8. Moynihan, B. G. A. Brit. M. J., 1903, 2: 1458.
9. Rekers, P. E., Pack, G. T., and Rhoads, C. P. Surgery, 1943, 14: 197–215.
10. Roeder, C. A. Ann. Surg., 1933, 98: 221–231.
11. Taylor, F. H. L., Castle, W. B., Heinle, R. W., and Adams, M. A. J. Clin. Invest., 1938, 17: 335–345.
12. Walters, W. The Stomach and Duodenum. Chapter 38. Philadelphia: W. B. Saunders Co., 1935.

TOTAL ABDOMINAL HYSTERECTOMY AND THE "OCCASIONAL OPERATOR"

EUGENE A. GASTON, M.D., F.A.C.S., Framingham, Massachusetts

TOTAL hysterectomy, as the operation of choice in the treatment of benign diseases of the uterus, has become increasingly popular during recent years. Hysterectomy with removal of the cervix is technically more difficult than without removal of the cervix, yet statistics from large gynecological clinics have shown the more radical operation to be little if any more dangerous (1–3, 8, 9, 12, 14–16, 20, 21). In these institutions the operations are performed by, or under the supervision of, surgeons who attain great technical skill by repetitiously performing the operation many times (in some cases several hundred times) each year.

It is proper that new surgical techniques should be developed and first evaluated in large clinics staffed by surgeons of experience. It is probable, however, that a large part of the total of pelvic surgery is done, not in such institutions, but in small community hospitals where operators are confronted with the problem of hysterectomy but a few times each year. The question arises as to whether the total operation should be advised for surgeons of such limited experience. The recorded opinions are of but one conviction. In fact, in the literature of no other operation has the "occasional operator" (variously estimated as the surgeon who does from 6 to 24 hysterectomies per year) been so consistently and emphatically warned against attempting to emulate the pioneers (2, 6, 10–12, 16–18, 20).

Phaneuf states: "In the hands of a well trained pelvic surgeon, who performs a hundred or more hysterectomies yearly, there is no great difference between the two methods in mortality and morbidity; but such is not the case in the hands of an operator who performs but few of these operations, probably 6 or 12 yearly." Similarly, Foss and Babcock state: "The surgeon who performs 1 or 2 hysterectomies a month should adhere to the supravaginal procedure. Such a man cannot consider himself broadly experienced. In all probability, the man who performs a hundred or more each year should be able to carry out the total operation expertly with a mortality no greater than that of the surgeon who adheres to the less formidable procedure." Even Phillips and Sears, whose series comprises only 32 cases of total hysterectomy, state: "The untrained and unexperienced will, of course, have a considerably higher mortality in total hysterectomy."

To a supposedly learned profession, advice to the effect that the surgeon should be conversant with pelvic anatomy, and with a satisfactory technique for removal of the cervix (11, 14, 16) may be regarded as superfluous. Given this fundamental background, the following study is presented in an effort to show that total hysterectomy may be safely utilized by the surgeon who does only an "occasional" hysterectomy.

From the Surgical Service of the Framingham Union Hospital, Framingham, Massachusetts.

GENERAL CONSIDERATIONS

In a practice limited to general surgery in a community of 25,000 population, the problem of hysterectomy has presented itself 130 times in a 7 year period ending May 31, 1944, an average of 18.6 hysterectomies per year. Of these 130 cases, 20, or 15.4 per cent of the entire series, were done by the vaginal route, all for procidentia, and 110, or 84.6 per cent of the entire series, by the abdominal route. Of the 110 abdominal hysterectomies, 39 were supracervical (35.5 per cent) and 71 were total (64.5 per cent). Of the total hysterectomies, 65 were performed for benign lesions and 6 for malignant growths. These 6 cases have been excluded from the present series because all are agreed that in situations which demand hysterectomy for the control of malignant growth of the corpus or of the adnexa, total hysterectomy should be done. Patients with such malignant lesions belong to an older age group and, from the very nature of their disease, are, in general, poorer surgical risks than the younger patients with benign pathology. It is not logical to include the malignant lesions with the benign in evaluating the risk of total hysterectomy done for benign disease, although this has been done in a great many of the reported series.

Table I shows the yearly distribution of supracervical and total hysterectomies in the 104 abdominal cases done for benign disease. The latter operation was first undertaken in January, 1939. During the succeeding 18 months, 11 total ab-

TABLE I.—YEARLY DISTRIBUTION OF ABDOMINAL HYSTERECTOMIES DONE FOR BENIGN DISEASE

	Number of abdominal hysterectomies	Supracervical hysterectomy		Total hysterectomy	
		No.	Per cent	No.	Per cent
Yr. ending May 31—1938	10	10	100.	0	0
1939	11	6	54.5	5	45.5
1940	16	10	62.5	6	37.5
1941	13	2	15.4	11	84.6
1942	18	3	16.6	15	83.4
1943	20	4	20.0	16	80.0
1944	16	4	25.0	12	75.0
Total	104	39	38.7	65	61.3

dominal hysterectomies were done for benign disease. The clinical impression was obtained that the postoperative reactions were not materially different from those encountered after supracervical hysterectomy. Thereafter, all abdominal hysterectomies done for benign disease were of the total type, unless contraindicated by the patient's general condition or by technical difficulties engendered by obesity or the pathology present. This attitude has been aptly stated by Vogt and Hamilton as follows: "We do not contend that all pelvic pathology should be treated with total hysterectomy, even when surgery is definitely indicated. Some pathology is grossly so overwhelming as to suggest discretion to the operator, and the few added minutes that might be required to remove a cervix in a patient already potentially shocked by a prolonged procedure, are not warranted."

On this basis, during the past 4 years, 80.6 per cent of the cases have been total hysterectomies. The apparent yearly reduction in the percentage of total hysterectomies during this time has not been due to any lessened enthusiasm for the operation, but is rather an example of the mathematical limitations of any small series of cases. For example, of the 4 cases of supracervical hysterectomy listed for the year ending May 31, 1944, one was in an extremely obese woman, with a deep pelvis and many adhesions from previous surgery, which made exposure difficult. The remaining 3 were done as emergency operations under less favorable circumstances; 1 for volvulus of an ovarian cystadenoma and 2 for acute exacerbations of pelvic inflammation in middle aged, married women, in whom in each instance a diagnosis of acute appendicitis had been incorrectly made.

TABLE II.—AGE DISTRIBUTION

	Supracervical hysterectomy		Total hysterectomy	
	No. cases	Per cent	No. cases	Per cent
20–29	7	17.9	0	0.0
30–39	10	25.6	14	21.6
40–49	16	41.1	35	53.8
50–59	5	12.8	15	23.1
60–69	1	2.6	1	1.5
Average age	40.05 yr.	(39 cases)	45.05 yr.	(65 cases)

Table II shows the age distribution of all cases of abdominal hysterectomy done for benign disease. As is true in all reported series, the majority of cases were done in the 4th and 5th decades. The average age of the supracervical cases was 40 years and of the total hysterectomy cases 45 years.

The indications for total hysterectomy as determined by the major pathological findings are as follows: leiomyoma, 37 cases, or 56.9 per cent; infection, 9 cases, or 13.8 per cent; endometriosis, 7 cases, or 10.8 per cent; adenomyosis, 3 cases, or 4.6 per cent; endometrial polyposis and hyperplasis, 4 cases, or 6.2 per cent; ovarian cysts, 2 cases, or 3.1 per cent; pregnancy complications, 2 cases or 3.1 per cent; perforation of uterus with intraperitoneal hemorrhage, 1, or 1.5 per cent. Chronic cervicitis was purposedly omitted from the diagnoses, since evidence of infection in the cervix was found in nearly all cases. Leiomyoma makes up the largest number, over half of this series, while leiomyoma, pelvic infection and endometriosis make up 81.5 per cent.

THE OPERATIVE PROCEDURE

It is not the purpose of this communication to describe the technique of total abdominal hysterectomy. Articles by Richardson, Farrar (4, 5) Bryan and Traube, Masson (11) Foss and Babcock, and Phaneuf are well illustrated. Geist has described a combined vaginal and abdominal technique. The technique used in this series is that described by Meigs by which accurate hemostasis during removal of the cervix is easily obtained. This is the most important single consideration in the entire operation. The surgeon who works under direct vision in a dry field has little fear of injuring the important surrounding structures.

Several points in the conduct of the operation seem worthy of emphasis. The importance of adequate preparation of the vagina has been

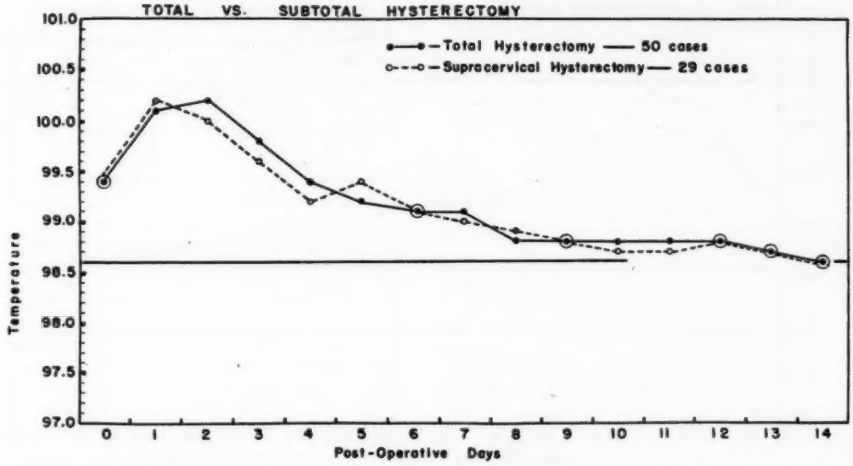


Chart 1. Average of highest daily temperature recordings in uncomplicated total and supracervical hysterectomies.

stressed by Farrar (3) who states that peritonitis will probably always remain a possible complication until the vaginal mucous membrane is as carefully prepared before operation as is the skin. This has been satisfactorily accomplished by placing the patient in the lithotomy position and thoroughly scrubbing the perineum and vagina with soap and water, followed by 70 per cent alcohol and aqueous zepharin. The bladder is then emptied with a catheter introduced under strict aseptic precautions. The uterus is curetted and, if infection or malignant growth is present, the cervix is closed tightly with a suture. Usually the cervix is not closed. If a minor amount of perineal relaxation is present, this is immediately repaired by a simple method requiring 15 or 20 minutes. If a second or third degree laceration requires a more extensive repair, this is deferred until after the abdominal hysterectomy has been completed. If the patient's condition is not ideal at the end of the abdominal operation, the perineorrhaphy may be deferred for several days. The importance of repairing even minor degrees of perineal relaxation at the time of, or soon after, hysterectomy, has not been sufficiently emphasized. In this series of 65 total hysterectomies, 36 (55.4 per cent) had the perineum repaired. Of these, 33 were done at the time of hysterectomy and 3 were delayed until about the end of the first postoperative week.

Due to the development of estrogenic substances which are effective when taken by mouth, the tendency in this series has been to be increasingly radical in the removal of the adnexa along with the uterus. Thus, in 64.6 per cent of the total hysterectomies, both tubes and both ovaries were removed, while this was done in only 48.5 per cent of the supracervical hysterectomies. Most of the supracervical cases were operated upon in the earlier years of the series. No complications related to removal of the adnexa have been encountered. The same may be said for routine removal of the appendix, which is always done if it can be easily delivered into the operative field. Appendectomy was performed in 47.7 per cent of the total and in 37.1 per cent of the supracervical operations in this series.

One of the objections that has been raised to total hysterectomy is the additional operating time required for removal of the cervix. In our series, the total time required to perform total hysterectomy including perineorrhaphy in 64 cases averaged 103.8 minutes; for the abdominal operation only, 73 minutes in 37 cases. Supracervical hysterectomy including perineorrhaphy averaged 87.7 minutes in 25 cases, and the abdominal operation only, 73.6 minutes in 14 cases. It should be noted that operating time in these cases means all of the time consumed from the time the anesthesia has been induced, until the dressing is in place. The average of all cases with records sufficiently complete for satisfactory analysis, shows total hysterectomy to require 16.1 minutes more than supracervical hysterectomy; yet 50.7 per cent of the former had immediate perineorrhaphy while this was done in only 11.4 per cent

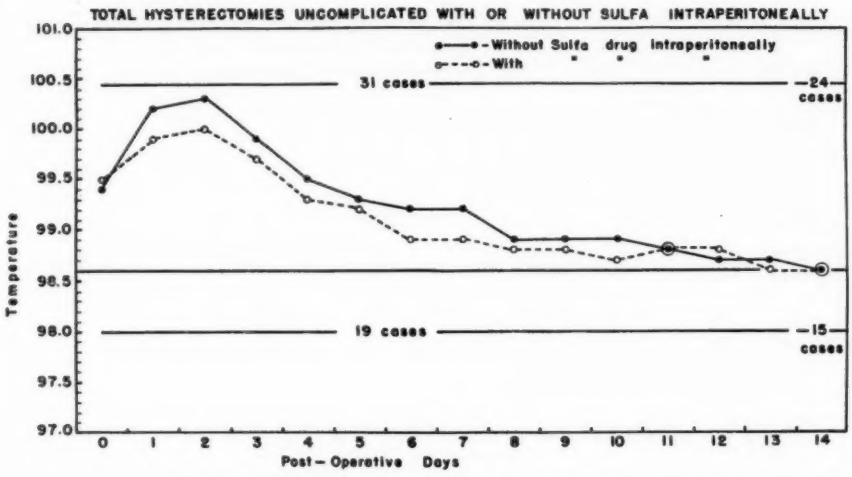


Chart 2. Average highest daily temperature recordings in uncomplicated total hysterectomies, with and without the intraperitoneal implantation of sulfa powder.

of the latter. Undoubtedly the time required for perineorrhaphy accounts for a large part of this difference.

In 37 cases of total and in 14 cases of supracervical hysterectomy, the anesthesia chart indicated accurately the duration of the abdominal operation, from the time the incision was started until the dressing was in place. While the number of cases is small, there is remarkably little difference in the operating time.

MORBIDITY

The average postoperative temperature reaction in 50 uncomplicated cases of total hysterectomy is compared with that of 29 similar cases of supracervical hysterectomy in Chart 1. It is evident that there is little difference between the two.

Chart 2 shows a similar comparison of uncomplicated cases of total hysterectomy with and without the application of 5 grams of sulfanilamide or sulfathiazole powder to the pelvic peritoneum. The clinical impression has been gained that those receiving the drug have had a somewhat easier convalescence. This impression is confirmed by the lower temperature reaction.

Table III enumerates the postoperative complications that have been encountered in this series. As expected, cystitis was seen most frequently in both the total and supracervical groups. The fact that it was seen twice as frequently after supracervical hysterectomy is of some interest. Probably the small number of cases in each group make this difference more apparent than real. However, during the past 3 years special attention has been directed to the postoperative care of the bladder, and this may also have played a part in the improved results. This care has consisted of constant urethral catheter drainage for a period of 4 to 7 days after operation. A real effort is made to keep the end of this catheter, and the attached drainage tubing, sterile. The bladder is thoroughly irrigated three times daily with a saturated aqueous solution of sulfanilamide heated to body temperature. After removal of the drainage apparatus, the bladder is emptied with a catheter, introduced under rigid aseptic precautions, every 6 to 8 hours, until the patient voids in amounts exceeding 6 ounces. Thereafter catheterization and bladder irrigation is done once daily until the residual urine is less than 1 ounce. Sulfadiazine in doses of 0.5 gram are given by mouth four times daily, starting the day after operation and continuing until a day or two after catheterizations have been stopped.

The remaining postoperative complications require little comment. The bleeding from the vagina in 1 case, following total hysterectomy, was not severe and responded promptly to the packing of the vagina with gauze. The only case of peritonitis followed supracervical hysterectomy done for chronic pelvic inflammation. Peritonitis in this case was of a low grade of virulence, was confined to the pelvis, and was followed by complete recovery.

FOLLOW-UP STUDIES

Of the 65 cases of total hysterectomy, 7 institutionalized patients have been excluded from the follow-up study. Of the remaining 58 cases, 56 have been personally examined from 2 to 66 months after operation. The average follow-up period was 23.2 months.

One case of postoperative ventral hernia developed during the first year after total hysterectomy. This caused sufficient symptoms so that operative repair was required and was followed by satisfactory healing. The abdominal wounds in the remaining 55 cases have remained well healed.

In a few cases a vaginal discharge has persisted after operation. In every case this has been found to be due to exuberant granulation tissue at the upper end of the vagina. Removal of the granulation tissue in the office followed by cauterization with silver nitrate has, in every case, resulted in prompt and permanent healing. The vaginal support in every case has been found to be satisfactory. There has been no prolapse of the vagina.

Particular attention has been paid to the length of the vagina at the time of the follow-up examinations. While accurate measurements of the elastic vaginal tube are not practicable, the clinical impression as to whether shortening has followed operation has been recorded in every case. In 4 cases (7.1 per cent) evidence of slight shortening was found. That this shortening was slight in amount and of no functional importance is indicated by the fact that 3 of these women were married and had experienced no dyspareunia as a result of the shortening. The fourth patient was unmarried. In none of the cases was persistent pelvic tenderness found, although this too was carefully sought for and recorded in every instance.

An effort was made to evaluate the effect of total hysterectomy on the sex life of each of the 43 patients whose husbands were living and well. Satisfactory information as to the libido before and after operation was obtained in 25 cases. Of these, 11 patients had a normal libido before operation of whom 8 found no change after operation. Six of these 8 patients had all ovarian tissue removed at the time of hysterectomy. Fourteen patients reported poor or absent libido before operation and all of these found no change after operation. Ten of these patients had all ovarian tissue removed. Thus 22 of 25 patients (88 per cent) found no change in libido. Of the 3 patients who found the libido lessened or absent after operation, 2 had both ovaries removed and the third had 1 ovary removed.

TABLE III.—POSTOPERATIVE COMPLICATIONS

Complication	Total hysterectomy (65 cases)		Supracervical hysterectomy (39 cases)	
	No. cases	Per cent	No. cases	Per cent
Cystitis	4	6.2	5	12.8
Deep thrombophlebitis (without embolism)	3	4.6	1	2.6
Superficial thrombophlebitis	1	1.5	0	0.0
Pulmonary embolism with recovery	1	1.5	0	0.0
Wound sepsis (superficial)	3	4.6	2	5.1
Pulmonary atelectasis	2	3.1	0	0.0
Bronchopneumonia	1	1.5	0	0.0
Surgical shock	1	1.5	2	5.1
Postoperative vaginal bleeding	1	1.5	0	0.0
Pelvic peritonitis	0	0.0	1	2.6

Information concerning orgasm before and after operation was obtained in 39 cases. Twenty-five patients reported satisfactory orgasm before operation of whom 20 (80 per cent) found no change after operation. Of these 20 cases 14 (70 per cent) had both ovaries removed. Of the remaining 5 patients all found orgasm absent after operation. Two attributed this to perineal pain, 1 to fatigue, and 2 to absent libido. Three of these 5 patients (60 per cent) had both ovaries removed.

Of the 14 cases reporting unsatisfactory orgasm before operation all stated that the same condition existed after the operation. Thus, of the 39 cases, 34, or 87 per cent, found that operation caused no change in the orgasm.

Thirty-five patients gave information concerning the presence or absence of dyspareunia. In none of these was dyspareunia present before operation. Five patients (14 per cent) stated that intercourse was painful after operation. All described the pain as located at the introitus. All of these patients had perineorrhaphy performed at the time of hysterectomy, and this probably accounts for the discomfort experienced. None of these patients showed evidence of pelvic tenderness or of shortening of the vagina.

MORTALITY

There were no deaths following either total or supracervical hysterectomy done for benign disease. One death followed total hysterectomy done for adenocarcinoma of the fundus, in a 69 year old woman. The patient was obese and had been bleeding for 11 months before entering the hospital. Death occurred on the seventh postoperative day following a septic course associated

with abdominal distention. Permission for autopsy was refused but, clinically, the patient appeared to have peritonitis. She was obviously a poor operative risk and treatment with radiation would have been better judgment.

SUMMARY AND CONCLUSIONS

A personal series of 65 cases of total hysterectomy done for benign disease is presented.

1. Important points in the conduct of the operation are emphasized.
2. Details of postoperative care are considered.
3. The morbidity and mortality rates of total hysterectomy are not significantly greater than of supracervical hysterectomy.
4. Follow-up studies indicate that about 85 per cent of patients subjected to total hysterectomy experience no change in their sex life. Significant shortening of the vagina does not follow.
5. The total operation may be safely utilized by the general surgeon of average experience.

REFERENCES

1. Bryan, W. A., and Traube, C. C. Ann. Surg., 1936, 103: 914–923.
2. Danforth, W. C. Am. J. Obst., 1941, 42: 587–593.
3. Farrar, L. K. P. Tr. Am. Gyn. Soc., 1939, 64: 248–259.
4. Idem. Surg. Gyn. Obst., 1935, 60: 827–839.
5. Ibid., 1938, 66: 44–54.
6. Foss, H. L., and Babcock, J. R. Surg. Gyn. Obst., 1943, 76: 214–227.
7. Geist, S. H. Am. J. Obst., 1937, 33: 1081–1086.
8. Harris, C. H. Texas J. M., 1938, 33: 618–623.
9. Jones, H. O., and Doyle, L. W. Am. J. Obst., 1943, 46: 160–169.
10. Masson, J. C. Surg. Clin. N. America, 1937, 17: 1131–1142.
11. Idem. Am. J. Surg., 1940, 48: 255–265.
12. McDonald, E. P. N. York State J. Med., 1939, 39: 503–508.
13. Meigs, J. V. Personal communication.
14. Miller, H. E., and Prejean, O. Am. J. Obst., 1941, 42: 580–586.
15. Nelson, H. M., and Weisberg, H. Am. J. Surg., 1939, 46: 348–352.
16. Pearse, R. L. Am. J. Obst., 1941, 42: 22–23.
17. Phaneuf, L. E. Surg. Gyn. Obst., 1944, 79: 182–191.
18. Phillips, J. R., and Sears, E. Am. J. Surg., 1941, 53:117–120.
19. Richardson, E. H. Surg. Gyn. Obst., 1929, 48: 248–256.
20. Tyrone, C. H. Ann. Surg., 1938, 107: 836–841.
21. Vogt, W. H., Jr., and Hamilton, E. G. Am. J. Obst., 1942, 44: 723–730.

CARCINOMA OF THE COLON

Producing Acute Intestinal Obstruction During Pregnancy

WILLIAM F. FINN, M.D., and JERE W. LORD, Jr., M.D., New York, New York

PREGNANCY complicated by carcinoma of the colon is fortunately so rare that authors of four standard books of obstetrics, Beck, De Lee, Stander, and Titus, do not mention it. Further evidence of the rarity of this lesion is given by the fact that Child and Douglas, who recently reviewed 120 operations performed in a group of 40,000 pregnant women at the New York Hospital, did not encounter a single case. Carcinoma of the rectum is more common and usually manifests itself by dystocia, while mechanical obstruction or peritonitis is commonly the first evidence of carcinoma of the colon in pregnancy.

Der Brucke, in 1940, reported 2 cases of carcinoma of the colon in association with pregnancy. In his first case signs of obstruction appeared in the 9th month of pregnancy. A 2,100 gram living infant was delivered after a medical induction. Laparotomy on the first postpartum day revealed a tumor which was composed of the lower part of the descending colon, the upper part of the sigmoid colon, the left tube, ovary, round ligament, and the left cornu of the uterus. Eight hours after the mass had been exteriorized, the patient died. Examination of the tumor mass revealed an adenocarcinoma of the colon which in addition to obliterating the lumen, had invaded the surrounding tissue and the left tube and the left ovary. Obstruction developed in his second patient in the 6th month of pregnancy. At laparotomy an indurated mass was felt in the sigmoid colon, cecostomy was performed, and a biopsy specimen of the omentum, showed metastatic adenocarcinoma. When premature labor ensued on the first postoperative day, a premature infant who weighed 3 pounds and 2 ounces and who died within 24 hours, was delivered. Two months later the patient died from cachexia and a terminal bronchopneumonia. Der Brucke further records 5 cases which he states are the only reports in the literature of the past one hundred years in which carcinoma produced obstruction during pregnancy. Three of these were due to carcinoma of the ovary, one, to carcinoma of the ileum, while only one was caused by carcinoma of the colon. This last case a summary of which was published in 1927 by Fairbairn, is incompletely reported, but in essence a carcinoma of the colon was discovered and removed shortly after the termination of a pregnancy of 7½ months' duration. Fairbairn in his original article does not mention the method of removal of the carcinoma or the outcome of the patient or child.

Evers, in 1928, performed a cesarean section because of a fixed mass which could be felt both vaginally and abdominally in the left half of the pelvis. At laparotomy this was found to be an inoperable carcinoma of the lowermost part of the sigmoid colon which was surrounded by enlarged nodes and which was adherent to the posterolateral aspect of the uterus. The baby was stillborn and the mother died on the 6th postoperative day of generalized peritonitis. There was a colloid carcinoma in the lower 4 inches of the sigmoid colon with metastases to the iliac and aortic nodes.

Mengert, in 1933, described a 30 year old woman who in the 9th month of her third pregnancy developed abdominal and flank pain. Because of a large mass which could be felt by rectal examination, a Porro cesarean section was done. A living 2,750 gram infant was delivered. The peritoneal cavity contained fibrin and pus. After death had occurred on the 3d postoperative day, postmortem examination revealed a perforated adenocarcinoma of the sigmoid colon which was located about 10 inches above the anus.

A similar case was described in 1937 by Fournier. After a labor of 2 hours this patient, a 31 year old quintipara, delivered a 3,200 gram living infant. Mechanical obstruction developed on the 3d postpartum day. Laparotomy revealed and postmortem examination confirmed the presence of peritonitis due to the perforation of an annular scirrhous carcinoma of the sigmoid colon.

The only recorded suggestions regarding management are made by Der Brucke and Berkeley (2). Der Brucke writes, "Recognized in the early months, the pregnancy should be disregarded and the neoplasm treated as under all other conditions. Recognized after viability, the fetus should be delivered from below and laparotomy per-

From the Departments of Obstetrics and Gynecology and of Surgery of the Cornell University Medical College and the New York Hospital.

Fig. 1. Preoperative flat plate of the abdomen which shows the site of obstruction in the sigmoid colon just below the left iliac crest.

formed for the correction of the obstruction immediately thereafter." Berkeley, Bonney, and MacLeod describe their management under four phases: (1) acute obstruction, (2) the presence of an operable tumor prior to the development of the obstruction, (3) an inoperable lesion without obstruction, and (4) dystocia. In the presence of an acute obstruction they recommend, regardless of the duration of pregnancy, hysterotomy, colostomy, and later resection. In the presence of an operable carcinoma uncomplicated by obstruction they suggest (1) colostomy and resection or (2) hysterotomy, colostomy and later resection, or (3) hysterectomy and resection. If the carcinoma is inoperable, but no signs of obstruction are present, they prefer hysterotomy and colostomy in the early months of pregnancy, while in the later months they recommend temporizing till viability, at which time a cesarean section and colostomy are performed. If dystocia is present, they prefer a cesarean section and colostomy.

CASE REPORT AND DISCUSSION

C. F., white, 31 years of age, tripara, quartigravida, was due on September 22, 1944. In 1928 at 15 she had rheumatic fever with chorea, but, at present, apart from mitral stenosis and insufficiency, she was well compensated and was classed II C (New York Heart Association classification). There was no history of diarrhea, constipation or bloody stools. Four days before admission in June, 1944, while in the 6th month of pregnancy, she developed recurrent cramps in the left flank which radiated downward and across the abdomen. She had not had a bowel movement for 2 days prior to admission. No flatus was passed; 2 enemas were given without return. Physical examination revealed a uterus which was enlarged to the umbilicus and which contained an active baby estimated at 1,500 grams. The upper abdomen was distended by dilated loops of bowel arranged in ladder patterns. Peristaltic waves were seen. The catheterized urine contained only a few white cells, the leucocyte count was 6 thousand and a flat plate of the abdomen (Fig. 1) showed loops of dilated bowel above a site of obstruction in the sigmoid colon. Acting on the diagnosis of a mechanical obstruction an exploratory laparotomy was performed by one of us (J.W.L. Jr.) on June 14, 1944. A left lower rectus incision was made under open drop ether anesthesia. The uterus was found to be 6 months gravid. The transverse and descending colon were dilated to twice their normal size and were slightly edematous. About 10 centimeters beyond the junction of the descending and the sigmoid colon was found a hard, annular lesion 2 centimeters in length. The bowel below this lesion was collapsed. There was no evidence of lymph node metastasis or of peritoneal implantation. Because of the extreme distention and the obvious carcinoma, it was deemed best to perform only a transverse colostomy at this time. Therefore, the left rectus incision was closed and the midportion of the transverse colon brought out through an upper right rectus incision. A rubber catheter was inserted into the colon for immediate decompression. Two weeks later the left lower rectus incision was opened, the uterus retracted toward the midline and an aseptic end-to-end anastomosis was done over Kocher clamps, with interrupted silk sutures, after about 15 centimeters of the sigmoid colon had been removed. After the anastomosis 4 grams of sulfanilamide were sprinkled into the peritoneal cavity and an additional 4 grams were placed in the layers of the wound which was closed without drainage by interrupted sutures of silk. Sulfadiazine had been administered for 24 hours prior to the resection and was continued during the first 7 postoperative days. The adenocarcinoma (Fig. 2) was an annular lesion which had produced complete obstruction. Histological examination of the accompanying lymph nodes failed to reveal any evidence of metastasis. Two weeks later on July 13, 1944, the colostomy was closed. Recovery from each of the operations was uneventful. No signs of premature labor appeared during any of these procedures, and 7 weeks after the first operation she was discharged and followed in the clinic where her obstetrical course was normal, until 1 month prior to term when she entered the hospital because of rectal bleeding. After admission the stools were mucoid, but were never grossly bloody. Because of the proximity to term, examinations of the colon were deferred and the patient was observed in the hospital until labor ensued. After a labor of 6 hours and 46 minutes a 3,360 gram infant was delivered. The puerperium was afebrile. Proctoscopy in the early puerperium revealed no lesion within 22 centimeters of the anus. Barium enema, however, showed an annular constricting lesion in the descending colon. Inasmuch as there was no mucosal defect, it was thought that this represented only the site of anastomosis, but further x-ray examination will be necessary to eliminate the possibilities of recurrence or spasm. Several nodules, measuring 1.0 by 0.5 centimeters, were felt in the diastasis of the rectus muscles. These physical and x-ray findings, while

not conclusive, are suggestive of recurrence or metastases. Hence our prognosis after delivery is less optimistic than it was at the time of resection.[1]

This case report emphasizes several surgical principles in the management of large bowel neoplasms during pregnancy. Child and Douglas have stated recently: "Pregnant women tolerate even major surgical procedures quite as well as the nonpregnant," and that "when the surgical disease, however, becomes complicated by peritonitis, the outlook is unfavorable, and the maternal and fetal mortality, high." This patient withstood the three stages which were necessary for the relief of the acute intestinal obstruction and the removal of the carcinoma of the sigmoid as well as any nonpregnant patient. Each wound healed satisfactorily and the total hospital stay was 7 weeks. The gravity of peritonitis in the pregnant woman led to the choice of the three stage method and the aseptic anastomosis. An alternate method would have been to perform a Mikulicz type of exteriorization of the loop of sigmoid with immediate resection and opening of the proximal loop for the alleviation of the complete obstruction. The method chosen was the closure of the left lower rectus wound as soon as the diagnosis was established and the immediate performance of a transverse colostomy. No contamination of the peritoneal cavity occurred because only gas was present in the transverse colon, whereas the sigmoid and descending colon contained formed feces.

Another point of importance in the management by the three stage procedure is the type of anastomosis of the sigmoid colon following the resection of the carcinoma. Many surgeons prefer the open side-to-side or open end-to-end techniques, but we have in practically all cases employed the aseptic end-to-end anastomosis over Kocher clamps with silk as the suture material. Wangensteen has stressed the value of such aseptic end-to-end anastomosis in operations on the colon. Because of the great danger of peritonitis in the pregnant woman, we believe that the aseptic technique contributed to this patient's uncomplicated convalescence. The great distention of the bowel above the carcinoma would have further contributed to the possibility of infection of the peritoneum, had an open anastomosis been done. A Mikulicz procedure would have been technically difficult because of the relatively short mesosigmoid and because of the large size of the uterus. Further, a secondary closure of the Mikulicz operation is not infrequently necessary, thus nullifying one of its assets—the one stage

[1]Patient symptom free 3 months postpartum.

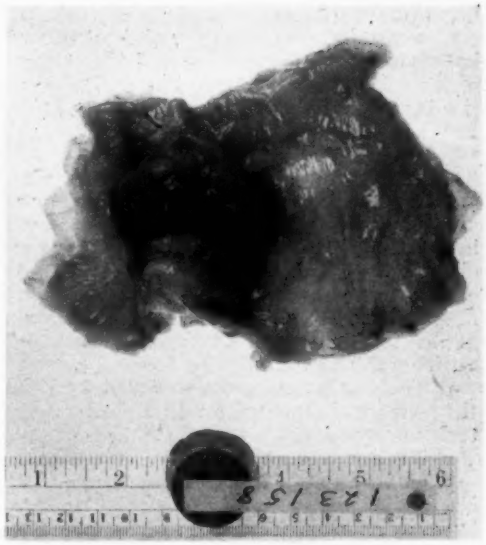


Fig. 2. Annular adenocarcinoma of the sigmoid colon.

operation. Though both Der Brucke and Berkeley state that the uterus should be evacuated either by vaginal delivery, hysterotomy, or hysterectomy, we found that the pregnant uterus did not interfere significantly with the technical performance of the operation. Experimental (11) and clinical (10) evidence indicate that the sulfonamide derivatives are of value in the prevention of peritonitis and of wound infection. Sulfanilamide was used at the time of the resection, both intraperitoneally and in the wound. Sulfadiazine had been given for 24 hours before operation and was continued for the first week after the resection.

Some authors have attributed the lack of early symptoms when carcinoma of the colon coexists with pregnancy either to the fact that the pregnancy masks the symptoms or they are mistakenly ascribed to the pregnancy. Our patient, however, had no symptoms until the acute obstruction developed. Christopher states that acute obstruction is the first manifestation in about 5 per cent of the patients who have carcinoma of the left side of the colon. From analyzing the few recorded cases, carcinoma of the colon may manifest itself in pregnancy by bowel symptoms which is rare, by obstruction as in our patient, by peritonitis, or by dystocia. The latter is most common if the carcinoma is low in the sigmoid colon where it joins the rectum. When the

first manifestation is peritonitis or dystocia, the outcomes so far recorded have been fatal. To our knowledge this is the first instance of carcinoma of the colon producing acute intestinal obstruction in pregnancy in which both mother and baby have survived.

SUMMARY

Because of its rarity and because of some unusual features in its surgical management, a case of carcinoma of the colon which produced acute intestinal obstruction during pregnancy has been discussed. For comparison all the reported cases of carcinoma of the colon complicating pregnancy have been briefly reviewed. To our knowledge our patient is the only one who has survived. We attribute this to the following facts:

1. The carcinoma first manifested itself by the presence of obstruction rather than by peritonitis or dystocia.

2. The carcinoma was in an operable state.

3. Multiple stage procedure was carried out, i.e., preliminary transverse colostomy followed by resection of the lesion and subsequent closure of the colostomy.

4. Aseptic anastomosis was performed.

5. Use of sulfonamide derivatives prior to, during, and after the resection was liberal.

REFERENCES

1. Beck, A. Obstetrical Practice. Baltimore: The Williams & Wilkins Co., 1942.
2. Berkeley, C., Bonney, V., and MacLeod, D. The Abnormal in Obstetrics. P. 120. London: Edward Arnold & Co., 1938.
3. Child, C., and Douglas, R. G. Am. J. Obst., 1944, 47: 213.
4. Christopher, F. Textbook of Surgery. P. 1177. Philadelphia: W. B. Saunders Co., 1939.
5. De Lee, J., and Greenhill, J. The Principles and Practice of Obstetrics. Philadelphia: W. B. Saunders Co., 1943.
6. Der Brucke, M. Am. J. Obst., 1940, 40: 307.
7. Evers, M. J. Obst. Gyn. Brit. Empire, 1928, 35: 525.
8. Fairbairn, J. Brit. M. J., 1927, 1: 456.
9. Fournier, R. Bull. Soc. obst. gyn. Paris, 1937, 26: 241.
10. Jackson, H., and Coller, F. J. Am. M. Ass., 1942, 118: 194.
11. Lord, J., Blakemore, A., and Stefko, P. Arch. Surg., 1943, 47: 352.
12. Mengert, W. Am. J. Obst., 1933, 26: 451.
13. Stander, H. J. Williams' Obstetrics. New York: D. Appleton-Century Co., 1941.
14. Titus, P. The Management of Obstetrical Difficulties. St. Louis: C. V. Mosby Co., 1940.
15. Wangensteen, O. Surgery, 1943, 14: 403.

DEFECT OF THE ANTERIOR MEDIASTINUM

Successful Surgical Repair

ROBERT E. GROSS, M.D., F.A.C.S., and JAMES E. LEWIS, Jr., M.D., Boston, Massachusetts

OPENINGS in the anterior mediastinum, with direct communication between the two pleural cavities, are very rare congenital abnormalities. Kupfer studied mediastinal lesions in 6,000 autopsies and did not observe such an anomaly. In 1939, Ochsner, DeBakey and Murray reported a case of congenital "absence" of the anterior mediastinum (associated with a left diaphragmatic hernia). They could find but 9 other reports of human subjects who were suspected of having a passageway connecting the two pleural spaces. We have reviewed the literature since that time and have uncovered no additional examples of the condition. In view of the rarity of the defect, it appears worthwhile to assemble pertinent facts which have been previously set forth by other authors and also to put on record a case which is apparently the first in which an anterior mediastinal opening has been surgically repaired.

SURVEY OF LITERATURE

In most of the previously described cases, "absence" of the anterior mediastinum caused little or no symptoms and was discovered only because there was evidence of a communication between the two pleural cavities. In 1903 Fraentzel observed at autopsy an individual with tuberculosis of the left lung who had sustained a spontaneous pneumothorax. A mediastinal opening had allowed air to escape into *both* pleural cavities, producing a bilateral pneumothorax and collapse of both lungs. In 1919, McCallum reported a case with tuberculosis of the right lung. During the production of an artificial pneumothorax, air was seen (by fluoroscopy) to pass also to the contralateral side. In 1924 Walsh and later Ioganson and Prozorov described 2 similar cases. In 1925, Dumarest and Bonafe reported the findings in a 35 year old man with tuberculosis of the left lung. After artificial pneumothorax treatment had been started on the left side, the patient complained of dyspnea and pain on the right side of the chest. Bilateral pneumothorax was evident by roentgenograms and was further attested to by aspiration of air from both pleural cavities. In 1930 Jullien studied a 24 year old woman with pulmonary tuberculosis. During injection of air into the right pleural cavity, the left lung became collapsed but the right did not. Apparently, the right lung was held to the chest wall by adhesions, but air could pass over into the left side of the thorax. Ameuille noted a similar situation in which lipiodol was introduced into the right pleural cavity and was then seen to pass anterior to the heart and to run over into the left pleural space. In 1933 Smith and Willis reported the findings in a tuberculous patient. Needles were introduced into both pleural cavities, and a rise in intrapleural pressure was noted during injection of air on opposite side.

In each of the instances cited, the presence of a pulmonary tuberculosis raises the possibility that an interpleural communication could have resulted from tuberculosis and necrosis of mediastinal tissue. In 1926, Le Wald made initial observations on a person with apparent interpleural communication, in the absence of demonstrable tuberculosis. This individual suffered a spontaneous right pneumothorax while "vigorously" using an adding machine. One week later, collapse of the left lung occurred, with evidence by roentgenogram of increased collapse of the right lung. It is not entirely clear whether this man actually possessed a mediastinal opening which allowed air to pass between the two pleural cavities or whether he sustained bilateral spontaneous pneumothoraces with an intact mediastinum. Ochsner, DeBakey, and Murray fully and clearly described anatomical findings which without question represented a congenital abnormality of the mediastinum. This 18 month old child was operated upon for a left diaphragmatic hernia. During the course of operation—by a transthoracic approach—an extensive and free communication was observed between the two pleural cavities. The entire anterior mediastinum was "absent," and a wide view of the right hemithorax could be obtained from the left sided chest wound. The pericardium and great vessels lacked their normal attachment to the posterior aspect of the sternum. The opening between the two pleural cavities was so large that, in effect, they constituted a single chamber. An identical malformation of the mediastinum existed in the patient herewith presented.

From the Department of Surgery of the Children's Hospital and the Harvard Medical School.

Fig. 1. Preoperative roentgenogram of chest, showing emphysematous right upper lobe. This lobe bulges over into the left side of the thorax (outlined by arrows).

Fig. 2. Preoperative, left anterior oblique roentgenogram following lipiodol injection. The right upper lobe is very emphysematous. The middle and lower lobes are compressed.

EMBRYOLOGIC AND ANATOMIC CONSIDERATIONS

The primary entodermal portions of the respiratory tree are developed in a median mass of mesenchyme, dorsal and cranial to the main peritoneal cavity. The original right and left stem buds of the lungs grow out laterally into their respective pleural cavities, carrying before them dome-shaped investments of mesoderm. As the lungs enlarge, they find room by burrowing into the spongy tissue of the adjacent body wall. This advance splits off an increasingly extensive pericardium from the thoracic wall and allows the lungs more and more to flank the heart on each side. When the pleural cavities are completed, the mesothelial coverings of the lungs become the visceral pleurae. The corresponding layers lining the thoracic wall constitute the parietal pleura. Before birth, the lungs are relatively small and compact. They occupy only the dorsal portions of the thorax, while the anterior mediastinum is quite extensive and is very broad. With the onset of breathing at birth, the lungs distend with air and assume a more anterior position—this readjustment taking place by compression and narrowing of the anterior mediastinum.

Fig. 3. Preoperative, lateral film of chest, showing anterior mediastinal defect. Wide, air-filled space between anterior border of pericardium and back of sternum.

The mediastinum lies between the right and left pleurae, in and near the median sagittal plane of the chest. It extends from the sternum in front to the vertebral column behind, and contains all the thoracic viscera except the lungs. It may be divided for purposes of description into two parts: the *superior mediastinum*, which lies above the upper level of the pericardium, and the *inferior portion*, which includes the structures and spaces be-

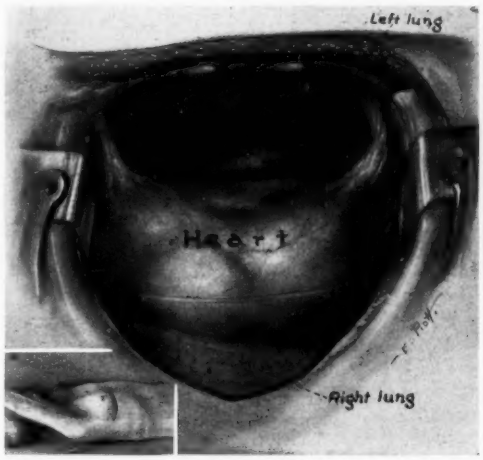


Fig. 4. Drawing of operative field. There is a broad opening between the sternum and the pericardium. When the chest was opened, the ballooned-out, right upper lobe was found prolapsed over through this opening. When this lobe was withdrawn, the operator could look directly over at the left lung, as shown in this drawing.

low the upper border of the pericardium. This lower portion is again subdivided into 3 parts, viz.: that in front of the pericardium, the *anterior mediastinum;* that containing the pericardium and its contents, the *middle mediastinum;* and that behind the pericardium, the *posterior mediastinum.* The anterior mediastinum is bounded in front by

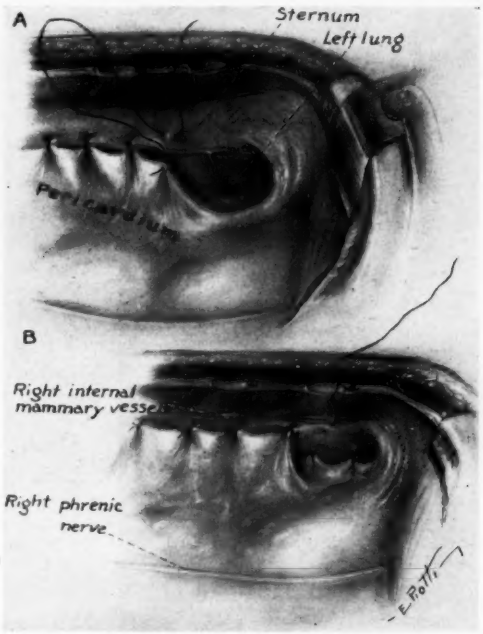


Fig. 5. Surgical repair of mediastinal defect. A, Pericardium and great vessels anchored to back of sternum with interrupted silk sutures. B, Second row of sutures being placed.

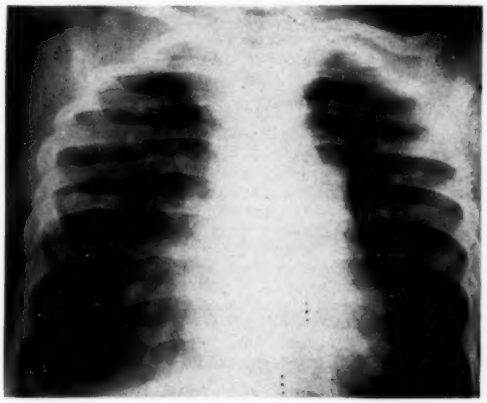


Fig. 6. Postoperative roentgenogram of chest. (Compare with Fig. 1.)

Fig. 7. Postoperative lateral roentgenogram of chest. The retrosternal space is now obliterated. (Compare with Fig. 3.)

Fig. 7.

Fig. 8. Photograph of patient 1 year after operation, showing excellent general physical status.

the sternum, laterally by the pleurae, and behind by the pericardium. It is narrow above, but widens out a little below. It contains a quantity of loose areolar tissue, some lymphatic vessels, scattered lymphatic glands, and the small mediastinal branches of the internal mammary arteries. The substance of the anterior mediastinum is such that it offers relatively little resistance to displacement and hence it may bulge to either side. Herniation through the mediastinum is a well recognized phenomenon and has frequently been seen in conjunction with lesions which disturb the normal pressure relationships on the two sides of the chest. Under such circumstances a lung which bulges into the contralateral side of the thorax is always covered by its parietal pleura.

Distinct from subjects with a mediastinal hernia are those rare individuals in whom an actual communication exists between the two pleural spaces. This latter, congenital type of anatomical curiosity is probably best explained on the basis of an over-encroachment of the lungs in a forward and then medial direction during fetal life, so that the yielding anterior mediastinum becomes compressed and resorbed. If such encroachment is of only moderate severity, a septum-like type of anterior mediastinum could presumably result—such as that normally present in the dog. If, however, the encroachment is more advanced, the pleurae which appose one another may disappear and an opening of variable size can develop between the two cavities.

A large communication between the pleural cavities, *per se*, probably causes no physiological abnormalities or clinical symptoms. Foundation for this statement can be found in the postoperative course of the patient described by Ochsner, DeBakey, and Murray, who had a repair of a left diaphragmatic hernia but no closure of the mediastinal opening. The child had no subsequent symptoms and roentgenograms showed no mediastinal or pulmonary shift. In contrast, a mediastinal opening is a definite hazard, if in addition there is some associated malformation or disease which disturbs the pressure equality which normally exists in the two sides of the chest. An example of such a mechanism is demonstrated by our patient who, in conjunction with the mediastinal opening, had a defective right upper lobe bronchus which allowed air to enter and then become entrapped in this lobe. This ballooned and the emphysematous lobe prolapsed through the anterior mediastinum and induced violent spells of respiratory distress.

CASE SUMMARY

In June, 1939, L. H., a 7 week old, white, female infant entered the Children's Hospital with a chief complaint of "difficulty in breathing" since birth. Delivery had been normal, but the baby was almost constantly cyanotic during the first few weeks of life. After that period, there were frequent episodes of rapid breathing, somewhat labored respiration, and concurrent cyanosis of moderate degree. These attacks varied in length from a few minutes to several hours. In the intervals between them, the child appeared to be normal in every way.

Physical examination revealed obvious respiratory distress. Breathing was rapid and strident in character, with definite intercostal retraction during the inspiratory phases. Crying would produce a moderate degree of cyanosis. On the left side of the chest, there was dullness to percussion and diminished breath sounds over the apex anteriorly and posteriorly; at the base, the sounds were harsh but otherwise normal in character. Throughout the right chest, particularly over the upper half, the percussion note was distinctly tympanitic; over the superior one-half of the lung the breath sounds were diminished and distant, while at the base they were of normal intensity and quality. The heart was markedly displaced to the left.

The white blood count was 13,000 cells per cubic millimeter. Red blood count was 4,600,000 cells per cubic millimeter. Hemoglobin was 95 per cent. Blood smear and differential count were normal. The urine was normal. MicroHinton test was negative. Tuberculin test (1: 1000) was negative.

Roentgenograms and fluoroscopic studies revealed an oblong, air-filled structure in the anterior and upper portion of the right pleural cavity, which extended over behind the sternum well to the left of the midline. Within the

periphery of this highly translucent area, a few indistinct, fine trabeculae could be seen—indicating that the structure was not a simple, air-filled sac, but that it contained some emphysematous pulmonary tissue. The lower one-third of the right pleural cavity and the outer two-thirds of the left pleural cavity contained lung tissue of normal aeration and density. The heart was displaced to the left. The roentgenographic picture suggested that we were dealing with a congenital cyst of the right lung, which communicated with a bronchus. Furthermore, the bronchus was thought to have a ball-valve obstruction, because air appeared to enter the "cyst" and become entrapped therein. The ballooning of the "cyst" toward the left was assumed to represent a true, anterior mediastinal hernia—that is, it was thought to be covered by parietal pleura as it bulged over through the mediastinum and to the left of the sternum.

On the fourth hospital day there was an especially severe episode of respiratory embarrassment which prompted aspiration of the "cyst" under fluoroscopic control. A needle was inserted through the right second intercostal space anteriorly and 90 cubic centimeters of air under considerable pressure were removed. This procedure, instead of improving the child's condition, caused cyanosis to become much more severe and indeed alarming. Fluoroscopy now showed that there was a bilateral pneumothorax. Apparently the needle puncture of the "cyst" wall had permitted air to escape into the right pleural cavity, and a portion of this air had passed over into the left pleural space. We now had indubitable evidence for the first time that a free communication existed between the two pleural cavities. In order to tide the baby over the current emergency, an intercostal catheter was quickly inserted into the right side of the chest and all free air sucked out of the pleural spaces.

On the 9th hospital day the thorax was explored by Dr. Thomas H. Lanman. Exposure was obtained through a right anterolateral approach in the fourth interspace. When the chest was entered, no cyst or accessory lobe was observed; instead, the right upper lobe of the lung was emphysematous to an extraordinary degree and represented the radiolucent structure which had previously been discovered by fluoroscopy and by x-ray film studies. This greatly distended right upper lobe ballooned over behind the sternum and protruded into the left side of the chest. When it was manually withdrawn from this location, an extensive defect or "absence" of the entire anterior mediastinum, from the diaphragm up to the sternal notch, was found. The pericardium and great vessels formed the posterior wall of this wide aperture between the two pleural spaces. The left lung could be viewed directly. Because of the exposure of both lungs to atmospheric pressure, the entire left lung and the right middle and lower lobes became quite collapsed. (The distended right upper lobe did not collapse, a fact which gave further evidence of some abnormality or valve-like mechanism in the right upper bronchus.) The baby's condition became so critical that it could be only partially controlled by the positive pressure, which was being administered through the anesthesia face mask. Because of the prostration of the child, nothing more was done, and the chest was quickly closed. The postoperative condition was precarious, but with sedation and use of an oxygen tent, the baby gradually improved. She was discharged on the 29th postoperative day.

The subsequent course of this child for the next 4 years was one of transient episodes of respiratory distress. These sometimes appeared two or three times a day; usually they occurred several times a week, but at some periods she was symptom-free for a month or more. Individual attacks listed from a few minutes to more than an hour. During these spells the respirations were very rapid and sometimes grunting and labored. The color became poor and mild to moderate cyanosis was often observed. The child would sometimes sweat profusely, and then after the attack would sink off into a deep sleep in an exhausted state. Unquestionably, there seemed to be an intermittent obstruction of the right upper lobe bronchus which temporarily permitted air to enter this lobe and distend it under considerable pressure. The enormous right upper lobe could then compress the remaining portion of the right lung and could also impinge upon the left lung to a lesser degree. A part of the picture may have been produced by direct pressure on the heart and great vessels. The child got no relief until in some way the valve-like action in the right upper bronchus was spontaneously released and the overdistended lobe was thereby deflated.

Frequent roentgenograms (Figs. 1, 2, and 3) showed a continuation of the picture previously described, consisting, in short, of: (1) A large emphysematous right upper lobe which extended over into the left pleural cavity; (2) atelectatic right middle and lower lobes; (3) some compression of the left lung; and (4) a shift of the heart to the left. In October, 1941, bronchoscopy and lipiodol study of the trachea and bronchial tree showed marked deviation of the trachea to the left and a very narrow right upper lobe bronchus. This latter did not appear to be compressed by external pressure; instead it seemed to be intrinsically stenosed, or else it was collapsed because of a congenital defect in its cartilaginous rings. The latter was thought to be the case, because on this basis the intermittent symptoms could be explained on entrapment of air whenever the unsupported bronchial walls flopped together and produced a valve-like obstruction. It seemed plausible that the child was suffering from a combination of two congenital malformations, namely: (1) an abnormal bronchus which permitted great overdistention of the right upper lobe, and (2) a wide defect of the anterior mediastinum which allowed the pressure effects to be transmitted not only onto the right middle and lower lobes, but also to the heart, the great vessels, and the left lung. Therefore, it was decided to reattempt correction of the existing congenital abnormalities, special precautions being taken with the positive pressure anesthesia to prevent bilateral pulmonary collapse when the chest was opened to atmospheric pressure.

Operation was undertaken on April 19, 1943 (by R.E.G.). The patient was now 4 years old. An intralaryngeal tube was passed down into the trachea to provide an adequate airway. A tightly fitting face mask provided a closed system through which cyclopropane was administered. The chest was opened anterolaterally in the 5th interspace on the right; the 5th and 4th costal cartilages were cut. After blunt and sharp dissection of existing adhesions, an excellent view of the interior of the thorax was obtained. The right upper lobe was quite emphysematous and protruded over through the anterior mediastinum into the left pleural cavity. When this was withdrawn, the left lung could be viewed extensively because of the great defect in the anterior mediastinum (Fig. 4). This hole was about 15 centimeters in length and ran the full length of the thorax. In anteroposterior dimensions it measured about 5 centimeters in its widest, central portion. There was no difficulty in keeping both lungs sufficiently inflated with the closed anesthesia system, employing positive pressure. The mediastinal defect was closed by drawing the pericardium and great vessels forward and suturing them with a row of about twenty interrupted, fine, silk stitches to the posterior surface of the sternum. The sutures grasped the sternal periosteum and then the pericardium or the areolar tissue in front of the pulmonary artery and aortic arch (Fig. 5). This vertical line of sutures was placed just medial to the left internal mammary vessels. A second row of stitches, similar and parallel to the first, was now placed about 2

centimeters to the right of the first, just medial to the left internal mammary vessels. This procedure resulted in a very satisfactory construction of the mediastinal septum.

A right upper lobectomy was now performed. The hilar structures were individually dissected and divided. The upper lobe bronchus was quite small and was not more than 4 or 5 millimeters in diameter. When freed adequately from overlying tissue so that it could be palpated, it was found to be soft and apparently devoid of cartilage in the section which was exposed. It could be seen to expand and collapse during the patient's respiratory efforts. Because of its soft and noncartilaginous structure, it was very easy to divide it and close it quickly with a single ligature. After the upper lobe had thus been removed, the middle lobe was allowed to turn upward so that a surface of it could be stitched over and buttressed against the stump of the upper lobe. When the thorax was closed, an inlying catheter was brought out through the chest wall for subsequent withdrawal of air and fluid. Gentle suction was applied to this catheter for 5 days, and it was then withdrawn. The postoperative course was entirely satisfactory. The temperature and pulse subsided to normal by the 6th day. The wound healed *per primam*. There was no empyema or bronchial fistula. The child was discharged on the 17th postoperative day.

During the year which has elapsed since operation, the patient has been entirely well and asymptomatic. A checkup roentgenogram on March 7, 1944, showed the heart in a normal position, the left lung fully expanded, and the right pleural cavity filled by the remaining right lower and middle lobes (Figs. 6 and 7).

In retrospect, one wonders if this patient might not have been cured by right upper lobectomy alone. While this possibility is freely admitted, it seemed to us at the time of operation that limitation of the surgical correction to lobectomy alone might be followed by subsequent distention of the left lung so that it would project over through the free space in front of the heart. In order to prevent any such future shift, it was felt that obliteration of the anterior mediastinal space was necessary to insure against any recurrence of respiratory difficulties.

SUMMARY

A brief review is given of previously reported cases of mediastinal defect and interpleural communication. Some embryological considerations are summarized as a basis for understanding a defect or "absence" of the anterior mediastinum.

An additional case report is made of a 4 year old child who had a large opening in the anterior mediastinum, a free interpleural communication and an anomaly of the right upper lobe bronchus. Deficiency of the bronchial cartilage allowed this airway to collapse in such a manner that air entered the upper lobe and became entrapped therein. Marked emphysema of the right upper lobe allowed it to protrude through the mediastinal opening and to invade the left pleural cavity. This child had intermittent attacks of severe respiratory distress, dyspnea, and cyanosis. These were completely relieved by simultaneous closure of the anterior mediastinal defect and removal of the anomalous right upper lobe. This is apparently the first recorded instance of surgical repair of an anterior mediastinal defect.

REFERENCES

1. Ameuille. Quoted by Jullien (9).
2. Arey, L. B. Developmental Anatomy. Philadelphia: W. B. Saunders Co., 1936.
3. Cummins, H. Quoted by Ochsner (17).
4. Dumarest, F., and Bonafe, L. Rev. tuberc., Par., 1925, 6: 104.
5. Emerson, C. P. Rep. Johns Hopkins Hosp., 1903, 11: 1.
6. Fraentzel. Quoted by Emerson (5).
7. Golden, T. Surgery, 1940, 7: 401.
8. Ioganson, L. F., and Prozorov, A. E. Borbas tuberk., 1932, 10: 172.
9. Jullien, W. J. méd. fr., 1930, 19: 392.
10. Korol, E. Am. Rev. Tuberc., 1938, 37: 39.
11. Kupfer, N. B. Proc. M. Ass. Canal Zone, 1923, 13: 136.
12. Lester, C. W., Cournand, A., and Riley, R. L. J. Thorac. Surg., 1942, 11: 529.
13. Le Wald, L. T. Arch. Surg., 1926, 12: 440.
14. Lewis, W. H. Gray's Anatomy of the Human Body. Philadelphia: Lea and Febiger, 1936.
15. Maier, H. C. Am. J. Roentg., 1938, 39: 687.
16. McCallum, A. Brit. M. J., 1919, 1: 305.
17. Ochsner, A., DeBakey, M., and Murray, S. Surgery, 1939, 6: 915.
18. Oechsli, W. R., and Miles, S. H. Am. Rev. Tuberc., 1934, 30: 239.
19. Smith, C. R., and Willis, H. D. J. Am. M. Ass., 1933, 101: 1224.
20. Tyson, M. D., and Crandall, W. B. J. Thorac. Surg., 1941, 10: 566.
21. Walsh, J. Am. Rev. Tuberc., 1924, 9: 337.
22. Werner, W. I., and Thearle, W. H. Am. Rev. Tuberc., 1942, 46: 105.

EDITORIALS

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MAY, 1945

ISABELLE HOLLISTER MARTIN

1863–1945

ISABELLE HOLLISTER MARTIN, the widow of Dr. Franklin H. Martin, passed away on March twenty-third. Mrs. Martin was born in Chicago at the corner of State and Washington streets on June 21, 1863, the daughter of Dr. John Hollister who was one of the founders of the Chicago Medical College which later became the Medical School of Northwestern University.

Throughout her life, Mrs. Martin was actively interested and engaged in the many activities of her husband and much of the credit for the success of this Journal was due to her encouragement and stimulation of the small group of young surgeons who met with Dr. Martin and to whom he outlined the aims and ideals of his new venture. Her home was a meeting place for these men and consequently she witnessed the birth of the idea of the Clinical Congress of Surgeons and later the American College of Surgeons and the Gorgas Memorial Institute. As a mother often feels, her greatest love was for her first born and as President of the Surgical Publishing Company following Dr. Martin's death she took an active part in the publication of the Journal until the time of her death.

Unassuming and modest, she had an alert, inquisitive mind and a habit of dissecting quickly to the heart of a proposal and stripping it of all the finery with which it had been painted with almost irresistible enthusiasm. She acted as a balance wheel of immeasurable value to Franklin Martin, and his invaluable contributions to his profession bear her unmistakable imprint.

STRICTURES OF THE COMMON AND HEPATIC BILE DUCTS

STRICTURES of the bile ducts are for the most part the result of surgical injuries to the common and hepatic ducts at the time cholecystectomy or operation upon the common bile duct is done. They are by no means uncommon. Dr. Cattell, of this Clinic, will shortly report on 124 reconstructions of the bile duct on patients sent to us for repair.

These strictures could more often be avoided by the application of a few reliably simple measures—better relaxation which can be provided by properly given and supervised spinal anesthesia; longer incisions which permit easier and wider exposure; rotation of the hepatic flexure, duodenum and pylorus to the left with gauze pads and retractors as we have described; good light focused on the deep hole

in which these structures lie; the individual demonstration and ligation of the cystic artery before the gall bladder is removed, and, finally, by the clear demonstration of the relationship between the cystic, common, and hepatic ducts before the cystic duct is clamped and cut. If these steps are carried out, there will be far fewer of these unfortunate calamities than there are now.

After having fought my way through a large number of these operations for reconstruction of an injured common or hepatic duct in patients who have had one, two, three, and recently five, unsuccessful previous attempts to repair the ducts, I would like to suggest that the highest percentage of good results in these cases can be obtained at the time of the first reconstructive operation. In practically all of the patients we have been able to find the lower end of the duct as it enters the duodenum and follow it upward to the stricture, but in many of the cases sent to us for repair, the previous attempts at reconstruction have so used up and destroyed the hepatic duct that the only remaining portion is intrahepatic and so quite difficult or impossible to use satisfactorily in its restoration.

Our best and lasting results have been obtained in the cases sent to us soon after the original injury. Our poorest results have been in those cases in which repeated, unsuccessful attempts have been made to reconstruct the injured duct.

There are a number of surgeons now in all parts of the country who have had experience with the reconstruction of injured bile ducts and so I can, I am sure, without suspicion of self-interest, urge that such reconstructive operations upon bile ducts not be undertaken without assessing one's ability to meet the technical difficulties occurring with them and without realizing that failure of the first reconstructive operation can make the second operation much more difficult and at times one in which it is impossible to obtain a satisfactory result.

FRANK H. LAHEY.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IT is generally agreed that medical history is a sorely neglected subject in the undergraduate curriculum. Students become doctors of medicine, oblivious, for the most part, of the great traditions of their profession. The little tome *Notable Names in Medicine and Surgery*[1] by Hamilton Bailey and W. J. Bishop affords an excellent opportunity for the popularization of medical history. While there is a tacit agreement among teachers that proper names associated with signs, symptoms, a procedure or an anatomical structure be ignored, the use of such names has persisted. Taking advantage of this, the authors have penned brief biographic and historical sketches of the personalities whose names are commonly known to students and practitioners because of the associations mentioned. With each sketch is a picture of the individual concerned and one or more appropriate figures. For example, the first section is fittingly concerned with Hippocrates and mention is made of the "Hippocratic oath" and "Hippocratic facies." Galen is next considered because of "The Veins of Galen," then Gabriel Fallopius because of the "fallopian tubes," etc. In the section devoted to Charles McBurney there are illustrations of the "point," the "incision," and the Roosevelt Hospital where he worked. Obviously such a work to retain the advantages of brevity, can not deal with all proper names that have been included in medical nomenclature. There are 81 sketches. The American reader will note the omission of Billroth (gastric resection), Mikulicz (operation), and Cushing (syndrome) when Carrel-Dakin (solution) and Böhler (splint) are included.

The authors deserve great praise for making available to the profession such a delightful, useful, and informative little book; the manner of presentation is original and greatly enhances its attractiveness for students. This volume should be made available to all medical students and should prove an important influence in awakening general interest in medical history.

ALEXANDER BRUNSCHWIG.

RADIOLOGISTS and others already familiar with the work of Brailsford welcome the third edition of *The Radiology of Bones and Joints*[2]. The ten years' interval elapsing since the publication of the first edition has seen attention focused on the recognition of early signs of various bone lesions and has permitted the author to correlate the onset and ultimate fate of the affected bones and joints in a manner which contributes much to the instructive value of the work.

Although the book is devoted almost exclusively to the study of bones and joints, due consideration is given the significance of certain other pathological changes in the soft tissues. The index is especially well prepared and deserves commendation. War necessities have made necessary the publication of many of the illustrations as line drawings. These appear in the text on relatively inferior paper, but the choice illustrations are reproduced very satisfactorily on proper coated paper. References to the literature have been brought up very well to date, including a satisfactory proportion of bibliographic references from the American literature. The text is exceptionally comprehensive, including a consideration of every bone condition and disease, whether congenital, traumatic, or pathological.

A particularly valuable phase of the author's text is revealed in his consistent effort to correlate the significance of the radiologic findings with the known facts of pathology.

JAMES T. CASE.

THE excellent book *Plaster of Paris Technic*[3] by Edward Geckeler covers the subject in a very thorough manner, beginning with the forms of plaster and explaining the general technique which is so essential to good cast application, and continuing with the various forms and types of employment. Each of the steps following the construction of the plaster bandage to and including the application, are pictorially elucidated. The errors and difficulties encountered are discussed and correction or improvements recommended. The various kinds of casts for different types of fractures and disabilities are not only discussed but are well illustrated. In my opinion this book is a contribution that is sorely needed, namely, teaching the undergraduates and graduates the correct technique of applying plaster. There is little that can be added, with the exception of the following constructive criticism:

1. In making molds or shells for the immobilization of fractures, the author states that one or two rolls are used. I do not believe that one or two rolls of plaster in a molded splint will efficiently immobilize the leg as the cast will be too thin in most instances.

2. In one of the illustrations on the immobilization of a forearm fracture, the subject has a ring

[1] NOTABLE NAMES IN MEDICINE AND SURGERY. By Hamilton Bailey, M.D., F.R.C.S., and W. J. Bishop, F.L.A. London: H. K. Lewis & Co. Ltd., 1944.

[2] THE RADIOLOGY OF BONES AND JOINTS. By James F. Brailsford, M.D., Ph.D., F.R.C.P., F.I.C.S. 3d ed. Baltimore: The Williams & Wilkins Co., 1944.

[3] PLASTER OF PARIS TECHNIC. By Edward Geckeler, M.D. Baltimore: The Williams & Wilkins Co., 1944.

on the fifth finger. Because of the danger of subsequent swelling, it is unwise to permit the patient to wear a ring on the injured arm or hand.

I highly recommend this book and believe that it will be beneficial to the medical profession.

JAMES J. CALLAHAN.

THE reader will find *The Urinary Tract*[1] by Kerr and Gillies a handbook of the more common and some of the uncommon lesions of the urinary tract, prepared for ready reference to the student, the practitioner, and the radiologist. Although emphasis is placed on the importance of correlating all the clinical and laboratory data with the roentgen findings before arriving at a final diagnosis, carrying out of this plan would lead to a too lengthy discussion of clinical and laboratory data and defeat the purpose of a book of this size. The text is divided into sections on the kidney, ureter, bladder, and urethra. Most of the printed material consists of descriptions and discussions of the illustrations on the pages following the text. The work is well arranged and the illustrations well chosen and reproduced. The scope of the work is remarkably complete considering its small size.

JAMES T. CASE.

IN spite of war conditions in England, the author of *Orthopaedic Surgery*[2] has been able to revise his book. The manuscript has been carefully gone over and new ideas have been incorporated both from personal experience and from the recent literature. Many operations that the author considers are no longer useful have been deleted. Among the sections which have been revised are those on circulatory disturbances, affections of the back, knee, shoulder, and foot, and infections of the hand. In all of these an attempt has been made to bring them up to date.

The author has incorporated some of Britain's ingenious operations on joints and Iselin's work on infection of the hand.

This volume is a compilation of a series of lectures and clinics on orthopaedic subjects which the author has given under the direction of Professor Fraser. He has drawn freely from recognized sources. He presents the material from the point of view of the general surgeon.

The Edinburgh Medical School maintains the tradition that a surgical specialty is a branch of general surgery and that to become a good specialist one must first be a good general surgeon.

An attempt has been made to present a comprehensive survey of each subject, including the latest work. The author has purposefully avoided the details of conflicting theories.

Some of the subjects covered are: congenital deformities; lesions and diseases of bones and joints; epiphyseal disturbances; affections of nerves; circulatory lesions of the extremities; complications of trauma; manipulative surgery; arthrodesis and arthroplasty. Various regions of the body are discussed especially spine, shoulder, knee, and foot.

No attempt has been made to give a comprehensive bibliography, but he does refer to authoritative articles on various subjects.

PHILIP LEWIN.

THE author of *Principles and Practices of Inhalational Therapy*[3] has compressed his long experience with gases for inhalational therapy into a small and very useful book. It should be available in hospital libraries for better understanding by the nursing and medical staffs of the physiological principles which are involved in gaseous therapy and of the methods which may be used.

The first paragraph on page 1 should be emphasized repeatedly in teaching medical and nursing students. Many instances of hypoxia and resulting irreparable cerebral injury could be avoided by providing an adequate airway to avoid partial respiratory obstruction and by use of additional oxygen, alone or in combination with helium or carbon dioxide.

A few minor changes in the text may be suggested. Figures 11, 12, and 14 (photographs of patients before, during, and after treatment) might be amplified by line drawings for clarity. More emphasis could be placed on the wide individual variations in oxygen consumption, as in hyperthyroidism where increased demand is a means of diagnosis. Toxic effects of carbon dioxide in a patient who is already deranged chemically and physiologically should be emphasized.

It is an excellent book. The bibliography includes many references to the author's articles. The descriptions and illustrations of equipment for gaseous therapy and for resuscitation are very good.

JAMES H. BENNETT.

A COMPILATION of the investigated works and studies of the peritoneum over an 18 year period is presented in *Infections of the Peritoneum*[4] by Bernhard Steinberg. As such, it is a correlation of the mass of experimental work that has been done on peritonitis by the author and the clinical management of the disease.

In the first three chapters, consideration is given to the mechanism of peritoneal infection, applied physiology of peritonitis, and the chemical changes in peritonitis. There follow chapters on pathology, progressive stages of infection, the peripheral blood, roentgen-ray diagnosis and treatment, acute peritonitis in children. The final chapters contain essentially clinical material, being devoted to special types of peritonitis as illustrated by case histories. The prevention and treatment of the disease are discussed in detail.

[1] THE URINARY TRACT; A HANDBOOK OF ROENTGEN DIAGNOSIS. By H. Dabney Kerr, M.D., and Carl L. Gillies, M.D. Chicago: The Year Book Publishers, Inc., 1944.

[2] ORTHOPAEDIC SURGERY. By Walter Mercer, M.B., Ch.B., F.R.C.S., F.R.S. Baltimore: The Williams & Wilkins Co., 1943.

[3] PRINCIPLES AND PRACTICES OF INHALATIONAL THERAPY. By Alvan L. Barach, M.D. Philadelphia, London, Montreal: J. B. Lippincott Co., 1944.

[4] INFECTIONS OF THE PERITONEUM. By Bernhard Steinberg, M.D. With a foreword by Frederick A. Coller, M.S., M.D. New York and London: Paul B. Hoeber, Inc., 1944.

The author gives a thorough exposition of the progress and method of development of acute peritonitis. He devotes special attention to such topics as exudation, absorption, distention, drainage, residual abscess, water balance, chemotherapy, and the use and effect of various drugs including a discussion of the sulfonamides.

The bibliography of peritonitis is a tremendous one, as any investigator who has worked with this subject can testify. In general practice, the disease often goes unrecognized in its early stages and is commonly improperly treated in all its stages. There is probably no disease about which we know so much for which we do so little in its later stage. For these reasons, and until a sharp reduction in mortality has been obtained, a volume such as this is an important contribution. The book is compact, well written, and contains an excellent bibliography.

J. R. BUCHBINDER.

IN the 5 years since the 6th edition of Flagg's *The Art of Anesthesia*[1] the war has speeded the progress of anesthesia, and the 7th edition is partially a report on this progress.

Dr. Flagg's observations have prompted him to reaffim his strong faith in ether as the backbone of anesthesia, and he calls for intensive and basic training in its skillful use, for both military and civilian medical men. He reports the frequency with which military men have turned to it in times of stress and hurry, finding it ready and reliable when other anesthetics were not. He says that " . . . its commonly accepted postoperative ill effects are due to maladministration . . . ," and its use will result in " . . . a lower morbidity, a better surgical field, and less embarrassment for the anesthetist."

Dr. Flagg criticizes the Army for its policy of allowing its newly trained anesthetists to exercise their judgment in each case, instead of teaching them a basic routine. He points out that the training period for these men is short and that it is naïve to think that they will be capable of intelligent judgment on the basis of their limited training and inexperience. In fairness to the anesthetist and his patient, the author suggests that training in the routine use of gas-oxygen-ether be given. He also considers harmful the Army order that the decision of the surgeon shall take precedence over the judgment of the anesthetist in the choice of anesthetic. It seems reasonable to believe that a surgeon's rank may not always qualify him to decide, and no anesthetist should be required to handle an anesthetic unfamiliar to him in an already trying and crucial situation.

The author believes that anesthesia is threatening to become a laboratory specialty limited in activity to the hospital. When the financially attractive hospital positions are filled, he fears for the teaching and practice of anesthesia, gas therapy, and life-saving methods outside the hospitals, and urges the training of the pneumatologist in general practice.

Beside the already well known and excellent chapters, there are new ones on the theory and technique of anesthesia with sodium pentothal, refrigeration, cyclopropane, and continuous caudal and continuous spinal methods. In regard to the latter he warns that most of the enthusiasts are the surgeons, who exult in the unlimited time given them, and he questions the wisdom of 6 and 7 hour operations with these methods.

There is an excellent chapter on fire hazard in anesthesia, and one titled "Our Wives and our Children—Who Shall Anesthetize Them?", which leads to the suggestion that the anesthetist consider his patient as he would a member of his own family in the same situation. While this is laudable, of course, the chapter might easily have been shortened, or left out altogether.

The new edition is valuable not only because it brings the book up to date, but because it avoids worthless controversial discussion, and spends its time on instructive technique and good advice from Dr. Flagg.

THOMAS H. COLEMAN.

THE second English edition (last German edition appearing in 1926) of Zondek's *The Diseases of the Endocrine Glands*[2] is certainly of value to the advanced student of endocrinology. The bibliographical material and the theoretical discussion are as usual of interest. The fundamental chemical and physiological work, both from a historical point of view and from a didactic point of view, is well presented. This edition, however, although coming into print in 1944, should be regarded as not quite up to date. Discussion of the function of the posterior pituitary, for instance, fails to include any reference to or mention of the work of Steven Ransom; discussion of the male hormone testosterone physiologically and clinically does not mention its most fundamental and important action, that of storing nitrogen in the somatic muscular system; a discussion of the thyroid diseases does not include any reference to goitrogenic substances such as thio-uracil. Despite these defects, this classic textbook remains a source of stimulation and valuable ideas.

M. P. STARR.

IT is the author's purpose in *Operations of General Surgery*[3] by Thomas G. Orr to accomplish the most difficult task of providing in one volume an operative surgery which contains the essential techniques in the field of general surgery. There can be no doubt but that Dr. Orr has achieved his goal in a most admirable fashion.

The charm of the book lies in its simplicity of presentation of proved and established operative procedures of general surgery and of most of its

[1] THE ART OF ANESTHESIA. By Paluel J. Flagg, M.D. 7th ed. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1944.

[2] THE DISEASES OF THE ENDOCRINE GLANDS. By Hermann Zondek, M.D. (German). Translated by Carl P. Giles, M.D., M.R.C.S., L.R.C.P. Baltimore: The Williams & Wilkins Co., 1944.

[3] OPERATIONS OF GENERAL SURGERY. By Thomas G. Orr, M.D. Philadelphia and London: W. B. Saunders Co., 1944.

specialties. Illustrations are profusely employed in a step-by-step manner leaving little to be desired.

It is not the purpose of the book to discuss preoperative and postoperative treatment or surgical pathology. Wherever necessary, however, there is a brief but adequate description of the anatomy of the region under consideration, and this is followed by a discussion of the dangers inherent in the procedure about to be undertaken. The techniques employed for each operation are discussed and when common disease is encountered, usually more than one approach is presented.

It is amazing that such an enormous amount of material can be covered in one volume. There is no space devoted to nonimportant information. For the general surgeon or the student, this book serves for a quick and satisfactory reference.

HILGER P. JENKINS.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

ESSENTIALS OF ALLERGY. By Leo H. Criep, M.D. With a foreword by Robert A. Cooke, M.D. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1945.

POET PHYSICIANS; AN ANTHOLOGY OF MEDICAL POETRY WRITTEN BY PHYSICIANS. Compiled by Mary Lou McDonough. Springfield, Ill.: Charles C. Thomas, 1945.

TRANSACTIONS OF THE AMERICAN NEUROLOGICAL ASSOCIATION; Seventieth Annual Meeting Held at the Waldorf-Astoria, New York, May 19 and 20, 1944. Richmond, Virginia: The William Byrd Press, Inc., 1945.

APPROVED LABORATORY TECHNIC; CLINICAL PATHOLOGICAL, BACTERIOLOGICAL, MYCOLOGICAL, VIROLOGICAL, PARASITOLOGICAL, SEROLOGICAL, BIOCHEMICAL AND HISTOLOGICAL. By John A. Kolmer, M.S., M.D., Dr.P.H., Sc.D., LL.D., L.H.D., F.A.C.P., and Fred Boerner, V.M.D. 4th ed. New York and London: D. Appleton-Century Co., Inc., 1945.

ANATOMY AS A BASIS FOR MEDICAL AND DENTAL PRACTICE. By Donald Mainland, M.B., Ch.B., D.Sc., F.R.S.E., F.R.S.C. New York and London: Paul B. Hoeber, Inc., 1945.

STUDIES OF BURNS AND SCALDS (Reports of the Burns Unit, Royal Infirmary, Glasgow, 1942–43). General Introduction, by L. Colebrook; Part I, by L. Colebrook, T. Gibson and J. P. Todd; Part II, by L. Colebrook, A. M. Clark, T. Gibson and J. P. Todd; Part III, by T. Gibson and A. Brown; Part IV, by A. Brown; Part V, by A. B. Anderson; Part VI, by T. Gibson; with Appendices. Medical Research Council; Special Report Series No. 240. London: His Majesty's Stationery Office, 1944.

LA RADIOLOGIA EN EL ESTUDIO DE LA VESICULA BILIAR. By Pedro A. Barcia. Buenos Aires: Librería y Editorial "El Ateneo," 1945.

LA RADIOLOGIA EN LOS DOLORES LUMBARES Y CIATICOS. By Dr. Mario A. Cassinoni. Buenos Aires: Librería y Editorial "El Ateneo", 1945.

NEURO-OPHTHALMOLOGY. By Dr. Donald J. Lyle, B.S., M.D., F.A.C.S. Springfield, Ill.: Charles C. Thomas, 1945.

LICÕES DE ANESTESIOLOGIA. Edited by Raul Briquet. São Paulo: Editôra Atlas S. A., 1944.

A TEXT-BOOK OF GYNAECOLOGY; FOR STUDENTS AND PRACTITIONERS. By James Young, D.S.O., M.D., F.R.C.S.E., F.R.C.O.G. 6th rev. ed. London: Adam and Charles Black, 1944.

PERIPHERAL NERVE INJURIES; PRINCIPLES OF DIAGNOSIS. Webb Haymaker, Capt., M.C., A.U.S., and Barnes Woodhall, Maj., M.C., A.U.S. Philadelphia and London: W. B. Saunders Co., 1945.

TEXTBOOK OF ANAESTHETICS. By R. J. Minnitt, MD. (Liverpool), D.A. (R.C.P.&S.Eng.), and John Gillies, M.C., M.B., Ch.B. (Edin.), D.A. (R.C.P.&S.Eng.). 6th ed. Baltimore: A. William Wood Book. The Williams & Wilkins Co., 1944.

MEDICAL GYNECOLOGY. By James C. Janney, M.D., F.A.C.S. Philadelphia and London: W. B. Saunders Co., 1945.

RADIOLOGIC EXAMINATION OF THE SMALL INTESTINE. By Ross Golden, M.D. Philadelphia, London, Montreal: J. B. Lippincott Co., 1945.

ESTUDOS CIRÚRGICOS. By Eurico Branco Ribeiro. 4 série. São Paulo, Brazil: Livraria Atheneu José Bernades, 1945.